Differential Equation Models for Aujeszky's Disease Virus in Irish Pig Herds

M.Sc. Thesis

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Declaration

I hereby certify that this material, which I now submit for assessment on the program of study leading to the award of Masters of Science in Applied Mathematical Sciences, is entirely my own work and has not been taken from the work of others save and to the extent that such work has been acknowledged within the text of my work.

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Contents

List of Tables

List of Figures

Abstract

Aujeszky's Disease virus, (ADV) is a contagious viral disease that affects the central nervous system of all animals, but swine are its natural host. Its main symptoms include abortions and stillbirths in sows, nervous signs in young pigs and respiratory disease in older pigs. ADV is a very important economic problem in Ireland, where substantial losses are incurred in the farming community each year.

We consider various differential equation models of ADV with homogeneous and proportional mixing between seropositive and seronegative animals. We derive various expressions for the basic reproduction ratio R_0, and the infectious contact rate, σ. Using these, we perform equilibrium and stability analysis for both *non-vaccinated* and *vaccinated* models. Finally, we look at various graphs of the systems of differential equations created, where we consider values, both above and below one, for R_0, σ. We find that it may be possible that the disease will die out by itself when $R_0, \sigma < 1$.

With the possibility of future trade restrictions being brought about by EU regulations, a nationwide eradication programme has been proposed. Ireland currently exports over 50% of its pigmeat, so any trade restrictions would have a huge economic impact. If the eradication programme is to be implemented, it is imperative that it be run efficiently, so as to minimise the possibility of the loss of valuable export revenue. Implications for control / eradication strategies are also considered.

Chapter 1

Introduction to Mathematical Modelling

1.1 Introduction

The purpose of this thesis is to mathematically study Aujeszky's Disease Virus (ADV) in Ireland. Aujeszky's Disease (AD) is a contagious viral disease that occurs in all animals, but swine are its natural host. AD is a very important economic problem in Ireland, where substantial losses are incurred in the farming community each year. In the U.S, the cost of AD is over $30 million each year [4]. We intend to study a mathematical model of AD and to come up with some future projections to establish whether the disease can be eradicated or not.

In Chapter 1, we briefly mention the mathematical theory of infectious diseases over the past two centuries, show Hethcote's model and mention the terms involved. Chapter 2 is a more detailed look at AD, its characteristics, economic importance and some Irish statistics relating to the disease. In Chapter 3 the main deterministic computations will be carried out and the stability will be analysed. Chapter 4 will look at the stochastic model and Chapter 5 the conclusions and possible extensions for future work.

It has been extremely difficult to obtain accurate data on AD as the last work done on it was in 1992, and this was just a study of why it should be eradicated. The only data that

we had to work with were those of [32] which is a model of human viral diseases, on which our model was based, and also [72] and [85]. As a result some parameters will be estimated using data from a recent pig report, [55]. Finally, before we begin this work, we give the floor to the medical doctor who, arguably, is the founding father of modern epidemic theory, Sir Ronald Ross, who wrote

> *'...All epidemiology, concerned as it is with the variation of disease from time to time or from place to place, must (sic) be considered mathematically, however many variables are implicated, if it is to be considered scientifically at all ... And the mathematical method of treatment is really nothing but the application of careful reasoning to the problems at hand.' [22]*

1.2 Review of Mathematical Modelling

First we show how mathematical theories of the spread of infectious diseases have developed. Then we will discuss the more recent work of Bailey [7]. This excellent book has covered deterministic and stochastic models, and we look at both. Recorded accounts of epidemic outbreaks and speculations go back as far as the ancient Greeks (Epidemics of Hippocrates $459 - 377$ BC) [7]. However, genuine progress in epidemiology was not achieved until more recently in the nineteenth century.

This such progress was made is due to the research of Pasteur (1822-1895) and Koch (1843-1910) in bacteriological science. People like Graunt (1620-1674) and Petty (1623-1687) first compiled medical and vital statistics in the seventeenth century. However, it was still too early for any theory on epidemics. Around this time the necessary mathematical techniques were only in the process of development and there was no sufficiently precise hypothesis about the spread of diseases suitable for expression in mathematical terms.

In 1760, Bernoulli used a mathematical method to evaluate the effectiveness of the technique of variolation (preventive inoculation) against smallpox, with a view to influencing public health policy. Evans (1875) used some curve-fitting methods on the smallpox outbreak of 1871-2, but this met with little success.

1.2.1 Deterministic Models

By the end of the nineteenth century the general mechanism of epidemic spread revealed by bacteriological research made some new developments possible. Hamer (1906) considered that the course of an epidemic must depend on the number of susceptibles and the contact rate between susceptibles and infectious individuals. These simple mathematical assumptions are basic to all subsequent deterministic theories. Hamer, by using these simple ideas, deduced the existence of periodic recurrences, an idea which was later taken up by Soper (1929).

Meanwhile Ross (1911) was working on a more structured mathematical model taking into account a set of basic parameters. From this model we can deduce the future state of the epidemic given the initial number of susceptibles, infectives and the attack, recovery, birth and death rates. For the first time it was possible to use a well-organised mathematical theory as a research tool in epidemiology.

In the 1920's Kermack and McKendrick, [45], [46], [47] considered the problem of endemic diseases and later developed more detailed and elaborate mathematical studies of the same type. Their most outstanding result was the celebrated Threshold Theorem [46], according to which, the introduction of cases into a community of susceptibles would not give rise to an epidemic outbreak, if the density of the susceptibles were below a certain critical value, the *threshold density*, N_T. If, on the other hand, the critical values were exceeded, then there would be an epidemic of magnitude sufficient to reduce the density of susceptibles as far below the threshold as it was originally above.

1.2.2 Stochastic Models

As epidemiological studies became more extensive and occasionally dealt with much smaller groups, the element of chance and variation became more prominent. The need for a probability model was becoming increasingly necessary. McKendrick (1926) was the first to publish a genuine stochastic treatment of an epidemic process. He assumed the probability of one new case in a short interval of time was proportional to the same quantity.

This is known as a 'continuous - infection' model which describes an individual to be infectious from the time that they becomes infective until they die, or recover. This did not attract much attention, but in 1928, Frost and Reed were doing similar work. Their model assumed that the period of infectiousness was short and that the latent and incubation periods could be regarded as constant. Greenwood (1931) also studied the same problem.

After World War II, deterministic treatments were carried further and stochastic developments increased following advances made in the mathematical handling of stochastic processes. Whittle (1955) developed a stochastic threshold theorem, in which a set of probability statements replaced the original Kermack and McKendrick model. The continuous - infection model introduced by McKendrick was reconsidered and it was shown that it could be used for analyzing household data as well as large - scale phenomena.

The treatment of simple stochastic epidemics continued and more detailed statistical analysis came to the fore. Improvements in obtaining the distribution of total epidemic size were given by Gani (1967) and Ohlsen (1964) extended the theory of parameter estimation and Weiss (1965) looked at the area of models involving carriers. The area of host - vector and venereal disease models was looked at by Bartlett (1964,1966).

Considerable effort has been devoted in more recent years to the elaboration of deterministic multistate models, which attempt to be more realistic than the models so far investigated. The modern approach tends to regard deterministic treatment to be approximately valid in certain circumstances, and in some cases may even generate the same results as the stochastic model. When the numbers of susceptibles and infectives are large and mixing is reasonably homogeneous, a deterministic model is likely to be sufficient.

Some of the more recent work on stochastic modelling has been done in [8], [53], [66], [83]. Even where stochastic modelling is preferred, it is always wise to start with a deterministic model as they may generate the same results.

1.3 Explanation of terms

The mathematical theory of infectious diseases has been extensively studied on human populations. Diseases such as AIDS, malaria and measles have all been studied previously. These diseases are known as SIR diseases where:

S = the number of susceptibles in the population (i.e, individuals who are capable of being infected with the disease)

I = the number of infectives in the population (i.e, the individuals who are infective and are capable of infecting the susceptibles)

R = the number of removed individuals in the population through either death, isolation or recovery(which means immunity).

1.3.1 Mathematical Interpretations

Usually, S, I and R are referred to as compartments in the overall population, which is usually N. Hence we can say

$$S + I + R = N \tag{1.1}$$

In general, populations show demographic turnover: individuals die for various reasons and new individuals appear by birth, immigration, etc. Such a demographic process has its characteristic time scale (for humans of the order 1-10 years). The time scale at which an infectious disease goes through a population is much shorter (e.g. for influenza it is of the order of weeks). For this reason we choose to ignore the demographic turnover and consider the population as closed [22]. With regards to AD modelling, more specific reasons related to pig farming must also be considered (these are discussed in more detail later).

1.4 Hethcote's Model

Hethcote [30], [31], [32], [33] developed various models for SIR diseases where recovery gives temporary immunity. The model we base our work on is from [32] and is as follows:

$$\frac{d}{dt}S(t) = -\lambda I(t)S(t) + (\delta_1 + \alpha_1) - (\delta_1 + \alpha_1)S(t) - \alpha_1 I(t) \tag{1.2a}$$

$$\frac{d}{dt}I(t) = \lambda I(t)S(t) - \gamma_1 I(t) - \delta_1 I(t) \tag{1.2b}$$

$$\frac{d}{dt}R(t) = 1 - S(t) - I(t) \tag{1.2c}$$

$$S(0) = S_0 > 0, \quad I(0) = I_0 > 0, \quad R(0) = R_0 \geq 0.$$

where,

λ = the daily contact rate between individuals,

δ_1 = the proportionality constant (the average lifetime is $1/\delta_1$),

α_1 = daily loss of immunity rate (permanent immunity occurs when $\alpha_1 = 0$),

γ_1 = daily recovery removal rate (the average period of infectivity is $1/\gamma_1$).

The number of contacts between I and S depends directly on the product of I and S, so this increases the number of infectives at a rate λIS, and therefore reducing the number of susceptibles by a corresponding rate. The number of infectives is then further reduced by the loss of immunity, α_1, and the recovery removal rate, γ_1. All parameters in (1.2) are nonnegative and only nonnegative solutions are considered as negative solutions have no epidemiological significance. Hence, there will always be a flow between the compartments in the model.

Another important aspect of the model in (1.2) is the fact that the population is consider to be closed, hence we can say, as we did in (1.1), that

$$S + I + R = N \tag{1.3}$$

where N is the size of the population, and is constant.

1.5 AD Model

The theory of infectious diseases in animals is very similar to the equations used above. The main difference is that an additional parameter, the harvesting parameter, must be considered. Harvesting is where the animals are killed for consumption, and this parameter play an important role in the model. For example, without knowing, a farmer could harvest the majority of his infected animals, thus reducing the spread of the disease, and in some cases, eliminating it completely.

The latent period has also be taken into account. During a latent period the disease goes into *hiding* in the animal and is undetectable. It then returns to make the animal infective again. The length of a latent period can range from a few days to several months, depending on the time of infection. Diseases such as Aujeszky's disease and Swine Fever in pigs, Bovine Tuberculosis (TB) and Brucellosis in cows are among these types of diseases. Bovine Spongiform Encephalopathy (BSE) in cows is another one of these diseases, but this is more difficult to model because of the human element (CJD).

The reason that we base our model on the equations in (1.2) is due to the fact that this is a model for herpes infections in humans and that ADV is a member of the alphaherpesvirus group [84]. AD is an example of a $SILI$ disease, where we define the new term L.

$$L = \text{the number of latents in the population (i.e. animals who are infected, but for a certain period of time they are unable to be infectious to susceptible animals).}$$

Another example of an $SILI$ disease would be Bovine Herpes Virus (BHV) in cattle herds [20]. The addition of a latent period makes the modelling of the disease more difficult. In standard SIR models, once an infection occurs, the next stage is recovery, through either death or immunity. However, with a latent period, there will be a flow between infective and latent for the lifetime of the animal. As one would expect, this flow will decrease over time, but given the relative short life span of animals bred for consumption, this is difficult to interpret accurately. This will be discussed in more detail in Section 3.2.1.

Of the more recent work done on AD a considerable amount is due to mathematicians and veterinarians from the Netherlands. Some of the most recent work can be found in [15], [18], [19], [73], [84] and [85]. In the Netherlands, AD is a disease of great economic importance due to the large scale pig production that occurs there. As a result, the rest of Europe is following the lead of the Netherlands in their efforts to eradicate AD.

Stochastic modelling has only recently been used in relation to AD. In some breeding units the numbers would be sufficiently small to require a stochastic model. Again, this is mostly done in the Netherlands, [20], [84]. We intend to look at both models, but we concentrate on the deterministic model as the number of pigs on a farm is usually large.

Chapter 2

An Overview of Aujeszky's Disease (AD)

2.1 Introduction

Aujeszky's Disease (AD) was first described in 1813 in cattle [38]. At that time the disease was unknown. Due to the intense irritation prior to death it was originally called 'mad itch'. It was not until 1902 that the disease was given its name, by the Hungarian scientist Aladar Aujeszky, when he distinguished psuedorabies from rabies [84]. As mentioned in Chapter 1, AD is a member of the alphaherpesvirus group of diseases (SHV-1).

Aujeszky's Disease, or pseudorabies (PRV) as it is also known, is a contagious viral disease that affects the central nervous system of most animals. Humans and the tailless apes (primates) are the only species that have immunity from AD [38]. Cattle, sheep, dogs and cats have been known to develop the disease. In these species it causes nervous signs, intense itching and is invariably fatal.

Its natural host is swine. They are the sole reservoir and usually the sole source of virus transmission [58]. Its main consequences are abortions and stillbirths in sows, nervous signs in young pigs, and respiratory disease in older pigs. Death rates can be high in young pigs, but as they get older, rates tend to diminish and this becomes less likely. Recovered pigs can act as a source of infection for uninfected pigs. These are important points with regards

to the development of the model.

In the USA raccoons are believed to be healthy carriers [90], [92] and in mainland Europe antibodies have been found in wild boar [70], [87]. The virus can also be spread by the wind (airborne infections), and infections of over three kilometers have been recorded [42].

2.2 Disease characteristics and clinical signs

The clinical signs of the disease can be described under the following headings [79]:

- Pigs less than three weeks old
- Pigs three weeks to five months
- Mature pigs
- Post-mortem lesions
- Immunity
- Spread of infection

2.2.1 Pigs less than three weeks old

In baby pigs, the disease may be characterised by sudden death with few, if any, clinical signs. Frequently death is preceded by fever, which may exceed 41°C, dullness, loss of appetite, vomiting, weakness, incoordination and convulsions. If vomiting and diarrhoea occur, the disease in baby pigs closely resembles transmissible gastro-enteritis (TGE).

In pigs less than 2 weeks old, death losses frequently approach 100%. Baby pigs may have become infected before birth and die within 2 days after birth, occasionally after showing violent shaking and shivering. Piglets infected immediately after birth may show clinical signs within the first 2 days of their life and they usually die before they are 5 days old. However, the influence of maternal antibodies does help reduce the transmission of ADV [13].

2.2.2 Pigs three weeks to five months

After 3 weeks of age, pigs have usually developed a degree of resistance to the disease, and death losses may decrease from 50% in pigs exposed when 3 weeks old to less than 5% in pigs exposed when 5 months old. Death losses vary with different strains of the virus, and even in grown pigs severe death losses occasionally occur.

Fever is a prominent clinical sign in these growing pigs and is followed by loss of appetite, listlessness, laboured breathing, excessive salivation, vomiting, trembling and eventually marked incoordination, especially of the hind legs. Normally death is preceded by convulsions. Involvement of the respiratory tract with sneezing, rubbing of the nose and coughing may occur. Clear to yellowish nasal discharges may be seen. Infected pigs that recover have lost condition and will be slow to reach market weight.

2.2.3 Mature pigs

The disease in adult pigs is usually not severe, but with some strains, deaths may occur. It is characterised by fever and respiratory signs, which may include nasal discharges, sneezing, nose rubbing and coughing. ADV is often found in conjunction with other respiratory diseases such as pasteurella and actinobacillus (hemophilus) pleuropneumonia. Nervous signs such as trembling, incoordination and itching occasionally occur, and blindness may follow pseudorabies infection. Vomiting and diarrhoea or constipation may be seen. Since 1980, an acute, often fatal pneumonia caused by ADV has increased in prevalence.

This condition is most often seen in herds having a prolonged history of pseudorabies infection. However, the majority of animals often die from a fatal secondary bacterial pneumonia as opposed to the disease itself. Sows infected in the early stages of pregnancy may return to heat because of death and resorption of their foetuses (where the body re-absorbs the foetus). Sows infected in middle pregnancy may eventually abort mummified foetuses, whereas sows infected late in pregnancy often abort or give birth to weak, trembling or stillborn pigs.

2.2.4 Post-mortem lesions

No gross lesions characteristic of pseudorabies are consistently found. Small greyish-white spots of focal necrosis may occur in the livers and spleens of pseudorabies infected young pigs. Congested pneumonic lungs are commonly seen. Virus isolation and fluorescent antibody examination of these and other tissues will reveal if the lesions are related to the disease.

2.2.5 Immunity

When ADV enters a pig, the pig's immune system recognizes that it is foreign. Specific cells in the humoral system produce antibodies that will try and kill ADV. When the disease is *removed*, these cells are no longer required and will decrease until only a few remain. These remaining cells are called *memory cells*, and their function is to remain in the animal in case ADV returns. If the disease returns, these *memory cells* activate the production of the antibody. If the animal has been previously exposed to ADV, the animal can respond much more quickly. The speed of this response will depend on a number of factors including age; nutritional state; health and, most importantly, the time elapsed since previous infection [37].

Recovery by swine from AD confers some resistance, sometimes for as long as twelve months. Re-exposure may result in reinfection, but it is usually asymptomatic. The passive immunity passed on from an immune sow to her offspring through the colostrum may protect the piglets for 5 to 10 weeks, after which they gradually become fully susceptible. However, the passive immunity may be too low to protect the piglets, hence the offspring of immune sows also may die of AD.

One of the reasons the disease continues to exist is due to the ability of the virus to establish a latent infection in pigs. During latency, the virus goes into *hiding* in the animal, and the animal appears healthy. However, the virus can be brought out of hiding during a process called reactivation [84]. Reactivation results in the shedding of the infectious virus causing its spread to uninfected animals. It has been shown that herds can be ADV positive for up to five years after a clinical episode, without obvious clinical problems [17]. It is this latent period / reactivation which makes the disease more difficult to model.

Recovered pigs may remain carriers of the virus and later can infect susceptible pigs or other animals with which they come into contact. Severe cattle losses from AD have occurred as a result of contact infection from apparently normal carrier swine. The disease also has occurred in swine farms by the introduction of carrier pigs. Vaccines have been used in Europe for years and in the United States since 1977 [34]. The research consensus is that vaccines reduce swine losses and spread of the disease, but do not totally prevent infection and the establishment of a carrier state in recovered swine.

Vaccines have been reported to enhance the control and eradication of AD [86]. They have precluded eradication for decades, because infected pigs could not be traced in vaccinated herds [75]. Newer 'differentiable' vaccines combined with their appropriate serological tests permit vaccinated animals to be distinguished from those infected with 'field' strains of the virus. Differentiable vaccines permit the monitoring of herd infection status in vaccinated herds.

2.2.6 Spread of infection

ADV is spread mainly by direct contact between swine; the nose and mouth are the main entry points for the virus [36]. Nasal discharges and saliva contain the virus; therefore, drinking water, bedding and other objects such as clothing and instruments may become contaminated. The virus can also be spread without movement of pigs; for this reason, when entering swine premises clean clothes should be worn, and boots should be disinfected upon entering and leaving the premises.

A higher density of pigs increases ADV transmissions under experimental conditions, owing to the higher number of contacts between animals. In a pig - dense region, i.e regions where there is more than one farm (these regions are quite common in Ireland), the contacts by area spread increase. This is due to the fact that there will a higher number of contacts between animals and as a result ADV may circulate more easily [75].

The virus also may spread by the movement of air within buildings and for short distances outside depending upon climatic conditions. Airborne spreading in late winter and early

spring is suspected to be over greater distances than previously thought. These airborne transmissions can be very difficult to contain in regions that have a high pig density.

2.3 Diagnosis and control

2.3.1 Diagnosis

Isolation of ADV can be made by inoculating a tissue homogenate, for example of brain tonsil or material collected from the nose / throat, into a sensitive cell line such as porcine kidney (PK-15) or SK 6, primary or secondary kidney cells. The specificity of the cytopathic effect is verified by immunofluorescence, immunoperoxidase or neutralisation with specific antiserum. The virus can also be identified using the polymerase chain reaction, but this technique is still new [23].

The clinical signs of AD are variable, so clinical diagnosis should always be confirmed by laboratory tests. Several tests, including the Serum-virus Neutralisation Test (SN), Virus Isolation (VI), Fluorescent Antibody Tissue Section test (FATS), the Enzyme Linked Immuno-Sorbent Assay (ELISA), and the Latex Agglutination Test (LAT) have been approved for the diagnosis of AD. Other tests are being developed. The SN, LAT, and ELISA tests detect ADV antibodies in serum of pigs that have been infected with the virus.

In a natural infection the disease lasts about $2-8$ days and the ADV antibodies appear in the serum about day seven of infection and may persist for years [36]. The presence of ADV antibodies is evidence that the pig has been infected with the virus in the past or has been vaccinated. Absence of antibodies indicates that the animal has probably not been infected or that it may be in the early stages of the disease. Diagnosis of an ADV outbreak can be made by conducting SN tests on paired serum samples, one taken from the pig early in the disease, and the next three to four weeks later.

A significant rise in antibodies between the first and second bleeding indicates active ADV infection has been present. The SN, LAT, and ELISA are extremely reliable tests. While these tests accurately detect antibodies to AD, they do not differentiate between antibodies

resulting from natural disease and those resulting from vaccination. Only the differential tests will permit such a distinction. Serum submitted for SN examination must be collected in clean, sterile tubes (not brucellosis tubes) and submitted packed in ice. If serum is badly haemolised or contaminated with bacteria, the SN test is unreliable.

2.3.2 Control of infection

The chances for introduction of the disease can be minimised if the owner strictly controls movement of people, animals and objects into swine premises, and if they have a number of rules/procedures implemented to protect the health of the herd. The application of the methods mentioned is known as *Biosecurity*, and it plays a very important role on the modern farm. Farms that have a good *Biosecurity* programme in operation can also reduce the prevalence of other diseases as well as AD.

Cats, dogs and all other animals should be kept well away from pigs. If new breeding stock is required, it should be added from a herd known to be AD-free, to avoid the risk of infection. Observations suggest purchased stock acts as a major source of virus introduction in a regional vaccination program [75]. All additional purchases should be tested and found free, isolated for at least thirty days, and then retested. Only then should they be allowed to enter the herd. Untested feeder pigs should never be brought onto premises where farrowing operations exist.

If AD occurs on a farm, the premises should be quarantined immediately, and all movement of animals and people should be strictly controlled. If at all possible, healthy animals should be separated from the infected ones, the problem here is identifying which animals are healthy. Dead pigs should be incinerated and recovered pigs should be sold only for slaughter to prevent the spread of infection around the farm and to other farms by carriers. The incineration of animals does not affect airborne transmissions due to the inability of the virus to survive in temperatures exceeding 24°C [5].

Due to the fact that Ireland has an island-based pig industry, we have a significant *Biosecurity* advantage over our European counterparts, and to some extent the UK. This was

reflected in the superior health status of the Irish pig industry when compared with that of mainland Europe (a summary is provided in Table 2.1, with the necessary amendments following recent outbreaks of Classical Swine Fever and Foot and Mouth disease in Ireland and the UK) [42]. A number of pig diseases that are still endemic on European farms have been eradicated from Irish farms. This should be of great advantage in the eradication of ADV as the possibility of secondary infections are greatly reduced.

Disease	Ireland	U.K	Europe
African Swine Fever	−	−	+
Anthrax	−	+	+
Aujeszky's disease	+	−	+
Classical Swine Fever	−	+	+
Foot and Mouth	+	+	+
PRCV	−	+	+
PRRS	−	+	+
Rabies	−	−	+
Swine Vesicular	−	−	+
TGE	−	+	+

Table 2.1: Comparison of health status: Ireland, U.K and mainland Europe

Another advantage that Irish pig producers have over their European counterparts is the intensity of the industry in Ireland. The majority of the producers in Ireland are intensive farming units, which means that only pigs are kept on the farm. This greatly reduces the possibility of transmissions to / from outside influences. This can be a disadvantage in pig-dense regions, as the contact rate (λ) is larger here than it would be on other, more isolated, farms.

It has been forecasted that margins in pig production will be greatly improved in period 2000/2001 [81]. This will be of immense relief to the industry, which has seen numerous setbacks over the 1998 - 2000 period. Among the others things forecasted were an increase in production costs and an increase in pigmeat consumption in the majority of EU countries [81]. If this forecast is correct, Ireland could see an increase in demand for pigmeat, which would emphasis the importance of disease control so that the consumers, both here and abroad, can have confidence in the industry.

2.4 Aujeszky's Disease in Europe

Only two countries worldwide with intensive pig production have managed to escape from ADV, Australia and Canada [48]. Every other country has had some prevalence of AD, some higher than others. The most intensive pig farming is done in mainland Europe and as a result the prevalence of AD is higher there than in most other parts of the world. With free trade within the EU, the spread of infection has become more difficult to contain [87].

To avoid future restrictions on free trade, member states need to achieve the same health status. Some countries have been more fortunate than others with regard to location, farming methods, climate etc., that all play an important part in the successful eradication of AD. At the moment the European countries can be divided into the following [87]:

- Officially AD free (OADF)
- Partially AD free (ADF)
- Infected Countries

2.4.1 Officially AD Free

Countries that are classified as OADF have been free of AD for at least two years. In these countries vaccination is not permitted. Presently, the following countres are OADF.

Denmark

Vaccination has never been used in Denmark [1]. An eradication program was put into operation in 1983 and it operated on a test and removal basis. The initial success rate was very good, going from 19% of infectives in 1983 to 1% in 1985. At the end of 1986 it was assumed Denmark was AD free as no ADV antibodies were found during serological examinations.

However, in the next few years various outbreaks were recorded. The main area was near the border with Schleswig-Holstein (Germany). This was due to the spread of airborne

transmissions from Germany as opposed to latent infections. Since Germany introduced compulsory vaccinations in this area no further outbreaks have been recorded.

Sweden and Finland

A national eradication program began in Sweden in 1991 [67], that was based on serological testing of all pigs older than 6 months. There were 230 outbreaks recorded in 1994. A serological survey carried out in 1996 showed 1% of the population was positive. The infected animals in question were slaughtered and Sweden was given OADF status in 1996 [68]. No outbreaks or clinical signs of ADV have ever been recorded in Finland [88].

Austria and ***Luxembourg*** are also officially free of AD [87].

2.4.2 Partially free of AD

United Kingdom

An official eradication scheme was put into operation in England in 1983 using test and removal [78]. Vaccination has never been permitted. Positive herds have decreased from 443 in 1983 to 5 in 1989. Since October 1989, ADV antibodies have not been detected in sera during serological screenings.

The situation in Northern Ireland is quite different. An eradication program began in 1994 and to begin with was quite successful. From meetings with officials from the Department of Agriculture for Northern Ireland (DANI), we have learned that at the present time there has been a series of setbacks, including an economic crisis in the pig industry. This has managed to make the tracing of seropositive animals extremely difficult and at the moment the current status of the scheme is unknown.

France

A national programme began in 1990 [87] and by the end of 1993 the prevalence had significantly decreased, and to date 21 administrative regions are officially free. The eradication

programme is regionally controlled and has been very successful. It is based on an accurate census of pig herds, results of preliminary serological surveys, control of animal movement, financial compensation, and on an administrative structure capable of applying these measures. In the remaining regions various eradication strategies are in operation ranging from intensive vaccination to test and removal.

To decrease the risk of clinical AD, some farmers randomly vaccinate the breeding herds with a systematical serological screening of finishing herds. In regions that have a high prevalence of AD a more intensive vaccination programme is advised. This policy has been progressively implemented since 1990. The aim is to clean up all the infected herds and, to achieve this, all herds selling piglets must undergo serological screening three times a year. A certificate of AD freedom is then issued.

Germany

Various control programmes are in operation in different regions ('Bundesländer') in Germany. To date several regions have OADF status, Thüringer, Sachsen, Brandenburg, Mecklenburg - Vorpommern, Saarland and Saschen-Anhalt [50]. Most of the other regions are infected [59]. In the areas along the border with Denmark (Schleswig-Holstein, Baden-Württemburg) vaccination has been mandatory, since 1990. Other infected areas include Lower Saxony (Niedersachsen) and Nordrhein-Westfalen.

All pig herds are serologically examined twice yearly to reduce costs. Following an outbreak of AD in an OADF region, the entire herd is slaughtered. In regions where ADV circulates, vaccination in breeding and fattening herds has been compulsory since 1991. In these areas animals with specific antibodies are slaughtered. These procedures have lead to a reduction from 23% in 1992 to 12% in 1993.

Wild boar have also been a complicating epidemiological factor. ADV antibodies were found in 1.7% of wild boar in Lower Saxony, Saschen-Anhalt and Brandenburg [70], [87]. It has yet to be shown if the wild boar in these regions will reduce the effectiveness of eradication. More information is needed before an assessment can be made.

2.4.3 Infected Countries

Belgium

A nationwide control program officially began in March 1993 [87]. It was decided a regional approach would be more successful as the majority of the pig industry in located in the north of Belgium (Flanders), where AD is endemic. In parts of south Belgium (Wallonia) the prevalence of AD is low.

Vaccination in mandatory in Flanders. The breeding stock is vaccinated either twice yearly with inactivated vaccines or three times with live attenuated vaccines. Breeding pigs are vaccinated three times and fatteners once, at the start of the fattening period. All vaccinations are recorded and a serological follow up is made. In Wallonia, vaccination is prohibited, except in cases that have a high risk of infection, or on farms where animals come from Flanders.

Nationwide screening is underway and will assess the prevalence of ADV in all regions. An official declaration of OADF will be offered to herds with complete gE (glycoprotein Enzyme) negative status.

Italy and Greece

A national control program was made compulsory in Italy in 1997 [93]. Most of the intensive pig farming is done in northern Italy (Lombary, Emilia - Romagna), where seroprevalence is high. In Greece, vaccination is performed on a voluntary basis [63], so the current prevalence of AD is unknown. Because Greece is a major importer of pigs, all imports are tested for ADV antibodies. Presently, an eradication programme is being considered.

The Netherlands

A nationwide eradication programme began in September 1993 [76]. The eradication has been split into three stages [15]. During the first stage, ADV transmissions were reduced, in the second stage, the remaining sources of ADV must be contained and eliminated. During the final stage, vaccination will be prohibited and test and removal will be used.

The Netherlands is the largest pig producer in mainland Europe that is not OADF. As a result, a lot of work, both mathematical and otherwise, has been done on AD. The recent work in [20], [77], [84] and [85] has been well documented. The majority of the eradication programmes in the rest of Europe have been widely based on the Dutch one. To achieve success in reducing ADV transmissions within and between herds, the following measures were imposed.

1. *Compulsory Vaccination*

All herd owners must vaccinate against AD. The breeding herd must be vaccinated three times a year, replacement pigs must be vaccinated three times before service and double vaccination is recommended for finishing pigs. Vaccination is done only by registered veterinarians and all vaccinations are recorded by the National Animal Health Service.

2. *Certifying herds free of AD*

In 1993 a voluntary program was implemented where herd owners could obtain ADF status [73]. This was done to reduce ADV transmissions. For ADF herds all gE- (gE delete) seropostives must be eliminated. Random sampling of the breeding herd is carried out three times and if no ADV antibodies are found the herd is declared ADF. After obtaining ADF status a certain proportion of the herd have to be tested at four month intervals to retain ADF status. In July 1990 450 herds were ADF [87].

3. *Surveillance of the gE- seroprevalence*

To monitor the eradication scheme a system has been designed for regional surveillance of gE- seroprevalence [76].

4. *Future Adaptations*

From monitored results, the risk of ADV introduction will be calculated at regional level. The outcome will be used to enforce double vaccination of finishing pigs in high risk areas. From January 1996 only ADF breeding herds will be allowed to move. Presently they are beginning to wind down their vaccination program, and hope to be OADF in two years [21], [76].

Portugal and Spain

Currently, preparations are underway to implement an eradication programme in Portugal [59]. Serological screening is being carried out and the results will be used to devise the control / eradication strategy that will be used.

Like France and Germany, Spain is divided into regions for eradication purposes. An official eradication program is prescribed in Galicia, Cataluna, La Rioja and Navarra. Eradication began in Galicia in 1992. Only gE- vaccines are allowed and all sows must be immunised. The vaccination of fattening pigs is done on a voluntary basis. Regular screenings make it possible to evaluate the ADV circulation.

Eradication began in La Rioja in 1991 and in Cataluna and Navarra in 1992. Only gE- vaccines are allowed. Again sows must be properly vaccinated and both inactivated and live attenuated vaccines may be used in fattening pigs. Serological surveys of breeders are carried out at slaughter to evaluate the progress made [87].

2.4.4 Eastern European Countries

Only recently has the prevalence of AD in Eastern European countries been calculated [56]. AD is, or has been, an important disease in most of these countries. To date, the Czech Republic, Slovenia, and the Republic of Estonia have become free of AD, while Hungary, Russia, and Slovakia, all have some form of eradication program in operation (the last is expected to be AD free in 2001 [56]). Other countries, such as Poland, Albania, and Bulgaria are all expected to begin eradicating very soon. Little is known about the prevalence of AD in the remaining countries.

2.5 Aujeszky's Disease in Ireland

Ireland is another country that is member of the infective group. ADV was first diagnosed in Ireland in 1960 [16]. Due to the intensity of the pig industry, AD increased in prevalence in the population. During the 1980's inactivated vaccines were licensed to try to control the spread of AD. They were replaced with gE delete inactivated vaccines and have now been augmented by the licensing of live gE delete vaccines.

AD is a scheduled and notifiable disease in Ireland [16]. A serological survey was carried out in July 1992 on 9041 sera from 310 breeding herds showed 7.5% to be positive [16]. From Tables 2.2 and 2.3 below (taken directly from [16]) we can get an idea of the prevalence of AD in Irish herds. The highest number and percentage of infected herds was in Tipperary (42%), Cavan (26.5%) and Cork (20.3%). Overall 7.5% of the samples were positive with 90.2% negative and the remainder inconclusive.

Herds	**No. Breeding (%)**	**No. Fattening (%)**	**Total (%)**
Positive	56 (18.1)	8 (26.7)	64 (18.8)
Inconclusive	41 (13.2)	1 (3.3)	42 (12.4)
Negative	213 (68.7)	21 (70)	234 (68.8)
Total	**310**	**30**	**340**

Table 2.2: Infection rate detected in Irish herds

% of Positive Sample herds	**Herds (Fattening)**
< 9	21 (2)
$10 - 39$	14 (1)
$40 - 99$	18 (2)
> 100	11 (3)
Total	**64 (8)**

Table 2.3: Estimation of the proportion of animals positive within infected herds

2.5.1 The Response to Vaccination

Vaccination of animals has been licensed in Ireland since 1983 [43]. A sample vaccination was carried out on a 12,000 pig fattening unit [40]. The incidence of AD seropositives in pigs fell from 96% before the commencement of vaccination in July 1994 (Table 2.4) to 15% just three months later (Table 2.5). By November, all serum samples in the fattening unit were tested, all were negative and have remained so subsequently.

Date	No. tested	No. positive	% positive
20.10.93	6	5	83.3
26.02.94	10	9	90
13.07.94	16	16	100
11.08.94	18	18	100
Total	**50**	**48**	**96**

Table 2.4: The incidence of AD seropositives *before* vaccination

Date	No. tested	No. positive	% positive
28.09.94	10	2	20
04.10.94	10	1	10
13.10.94	10	1	10
16.11.94	17	0	0
19.11.94	26	0	0
02.12.94	10	0	0
21.12.94	10	0	0
10.01.95	10	0	0
Total	**113**	**4**	**3.5**

Table 2.5: The incidence of AD seropositives *after* vaccination

Kavanagh, [44], extrapolated these figures to that for a National Herd of 160,000 sows, and found that 20% were AD positive, 75% were vaccinated and 5% had circulating virus. Seasonal variations in pig performance were accounted for by examining similar periods in each year. The estimated cost of AD was £0.51 per pig based on a purchase weight of 32kg and a sale weight of 97kg [44], [49].

2.5.2 Proposed Eradication Programme

The proposed eradication scheme for Ireland will classify the herd status into five levels [16]:

- Officially AD free (OADF)
- AD free (ADF)
- Monitored Herds (MH)
- Infected Herds (IH)
- Non-Status Herds (NSH)

Herds that are OADF must have not been vaccinated for at least two years and must have had a full herd blood test with negative results. ADF status herds are similar to OADF, except that vaccination is permitted. For MH, a statistically valid sample of the herd is tested with negative results. Here vaccination is optional. In status IH, vaccination is mandatory as positive animals are detected. With NSH no information is available about the herd. It is intended that NSH do not remain in this status for very long.

If we look at Table 2.6 below, we can see that Ireland is one of the larger pigmeat exporters in the EU that does not have some sort of eradication scheme in operation [54]. Indeed, 50.9% of the pigmeat produced in 1999 was exported [3]. From this we can gather that a scheme should be implemented immediately. If this is not established the closure of valuable export markets seems inevitable. This would have severe financial effects on an industry already suffering from falling pigmeat prices.

European Country	Production as a % of Consumption
Denmark	425
Netherlands	275
Belgium	187
Ireland	145

Table 2.6: Pigmeat production in selected European countries

2.5.3 Eradication Costs / Procedures

Kavanagh [40] conducted an investigation into the cost of an AD outbreak in a 370-sow herd selling fattening pigs. He estimated that the cost of an AD outbreak to be in the region of £9000 per 100-sow herd size. Where sows are vaccinated, the risk of a clinical outbreak of AD in the breeding herd is low, hence the cost of AD is primarily limited to that associated with virus circulation in weaners or finishing pigs. It is thought that twice yearly vaccination of breeding stock with inactivated ADV vaccines is capable of controlling the clinical signs of AD [41]. However, it may fail to eradicate ADV from the population.

More recently, some work by [44] has shown that AD can be detected by modifying the ELISA test and analysing the meat juices after the pigs have been harvested. With the proper marking, it would be possible to tell from which herd the infected animals originated. If all herds could be monitored for circulating virus on an ongoing basis, and strategic control programmes introduced on farms with circulating virus, then virus circulation could be eliminated. As mature seropositive sows were replaced by seronegative gilts, the virus would be eventually eliminated.

Recent research into eradicating AD at farm level has shown the cost of AD in an IH is approximately £0.50 per pig in a 5,000-place pig finishing unit. AD can be eradicated from finishing herds in four months, where almost all animals were seropositive at the beginning [44]. From this a break-even point would be reached approximately nine months following the completion of an eradication programme. Therefore, there are very significant economic advantages to be gained by eradicating AD from finishing herds. There is also the possibility for co-financing within the context of EU Council Decision 90/424/EEC on expenditure in the veterinary field, which would greatly reduce the costs incurred during an eradication programme [91].

At the present time, government legislation is underway to introduce the Aujeszky's Disease Order. This should then bring about the introduction of an eradication scheme. From communications with department officials and members of the IFA (Irish Farmers Association), this was proposed to commence in the spring of 2001. However, with the recent outbreak of Foot and Mouth Disease in Ireland, it has been put off until June 2002. From the infor-

mation above, any scheme introduced should be well organised. An efficiently run scheme could be very successful in the tracing and removal of infectives from the population and eventually lead to the eradication of AD.

Unfortunately, the current BSE crisis in Ireland and Europe has had a twin impact on pig producers. The ban on meat and bone meal inclusion in animal feeds in Europe has already increased soya bean meal prices and pig feed prices. Secondly, the demand for pigmeat is not forecast to rise to the same extent as happened following the 1996 BSE crisis [82]. In the likely event of a continuation of the BSE crises, it is unknown the effect that it will have on the pig industry. If demand was to increase, then the need for ADV to be eradicated would be doubly important, as the pig industry would need to take full advantage of any short term market increases.

Also, due to the recent difficulties in the industry, a number of the smaller producers are no longer in existence. This makes the control of animals much easier, and hence would ease the administration of the implementation of a vaccination scheme. As mentioned previously, it is only a matter of time before economic sanctions are introduced by the EU. This would be disastrous for the Irish pig industry. With the mathematical models that we will develop in the forthcoming chapters, we hope to be able to find the appropriate parameters to attack, with the intention of finding the most cost effective and efficient way of eradicating ADV.

In light of a renewed interest in ADV, and our lack of suitable Irish data, it was decided that a Nationwide questionnaire could be created, to gather information for both our work and the Department of Agriculture. An outline of what was proposed to the Department and the Irish Farmer's Association is contained in Appendix B.

Chapter 3

Deterministic Model

3.1 *SIR* model

Before moving on to the *SIL* model, we develop some important concepts in the basic *SIR* model,

$$\frac{d}{dt}S(t) = -\lambda IS \tag{3.1a}$$

$$\frac{d}{dt}I(t) = \lambda IS - \beta I \tag{3.1b}$$

$$\frac{d}{dt}R(t) = \beta I \tag{3.1c}$$

where

$$S + I + R = N$$

N = the size of the population, which is constant

λ = the daily contact rate between individuals

β = the daily removal rate.

A considerable amount of work has been done on the equations in (3.1) [7], [14], [22]. In (3.1) the expected duration of the infectious period is $1/\beta$ and a force of infection λ is inserted on all susceptibiles, which is N to begin. From this we can show the reproduction ratio to be

$$R_0 = \frac{\lambda N}{\beta}. \tag{3.2}$$

The reproduction ratio will be discussed in more detail later. (Section 3.3). From (3.1) we conclude that I initially grows with rate $\lambda N - \beta$. Hence we define the *initial exponential growth rate* as

$$\begin{aligned} r &= \lambda N - \beta \\ &= \beta(R_0 - 1). \end{aligned} \tag{3.3}$$

We can calculate the *initial growth rate* as

$$I(t) \simeq \lambda e^{rt} \tag{3.4}$$

where r is the *initial exponential growth rate* and λ is as before. We define $i(t)$ as the *incidence*, i.e. the number of new cases per unit of time. ($i(t) \simeq dI/dt \simeq e^{rt}$).

New cases at time t result from contacts with infectives that are infected at time t. We have the following equation for the *incidence* in the initial phase of an epidemic

$$i(t) = \lambda p \int_{T_1}^{T_2} i(t-\omega) d\omega \tag{3.5}$$

where, p is a probability $\in (0,1)$, ω is the *infection - age*, i.e., time since infection took place, and the infectious period has length $T_2 - T_1$. Using (3.4) we can write (3.5) as

$$1 = \lambda p \int_{T_1}^{T_2} e^{-r\omega} d\omega \tag{3.6}$$

Then we can conclude that there exists a unique real root r, i.e. equation (3.6) tells us what the exponential growth rate is. $r > 0$ iff $R_0 > 1$ and vice versa. In words, we will only have growth in real time if and only if we have growth on a generation basis (if $r = 0$, $R_0 = 1$). If an epidemic has growth rate r, we can calculate the *doubling time*, i.e. the time it takes for the epidemic to double as

$$T_d = \frac{\ln 2}{r} \tag{3.7}$$

and from (3.3) we can see that the *threshold density* can be calculated as

$$N_T = \frac{\beta}{\lambda}. \tag{3.8}$$

If the number of susceptibles is below a critical value, the introduction of an infective will not give rise to an epidemic outbreak. This critical value is known as the *threshold density.*

From (3.8) we can say that below N_T we have $R_0 < 1$ and above it, we have $R_0 > 1$. This will be discussed later in Section 3.3.3. The first two equations in (3.1) do not depend on R and we may consider these separately from the third:

$$\frac{d}{dt}S(t) = -\lambda IS \tag{3.9a}$$

$$\frac{d}{dt}I(t) = \lambda IS - \beta I. \tag{3.9b}$$

The orbits of (3.9) are the solution curves of the first order equation

$$\frac{dI}{dS} = \frac{\lambda IS - \beta I}{-\lambda IS}$$

$$= -1 + \frac{\beta}{\lambda S} \tag{3.10}$$

$$\Rightarrow dI = \left(-1 + \frac{\beta}{\lambda S}\right) dS. \tag{3.11}$$

Integrating (3.11) and rearranging, we have, for some constant C,

$$C = \frac{\beta}{\lambda} \ln S(t) - S(t) - I(t) \tag{3.12}$$

and we can say (3.12) is independent of t. Then we write (3.12) as

$$I(S) = I_0 + S_0 - S + \frac{\beta}{\lambda} \ln \frac{S}{S_0} \tag{3.13}$$

where S_0, I_0 are the initial number of susceptibles and infectives at time $t = t_0$. Note: $S_0, I_0 > 0$, as mentioned in Chapter 1.

To analyse the behaviour of the curves of (3.9) we use (3.10). From this we can say that (3.10) is negative for $S > \beta/\lambda$ and positive for $S < \beta/\lambda$. Hence, $I(S)$ is an increasing function of S for $S < \beta/\lambda$ and is a decreasing function of S for $S > \beta/\lambda$. We observe that $I(0) = -\infty$ and $I(S_0) = I_0 > 0$.

Then there exists a unique point S_∞, with $0 < S_\infty < S_0$, such that $I(S_\infty) = 0$, and $I(S) > 0$ for $S_\infty < S \leq S_0$. The point $(S_\infty, 0)$ is an equilibrium point of (3.9) since both S' and I' vanish when $I = 0$. Thus the orbits of (3.9), for $t_0 \leq t < \infty$, take the form described in Figure 3.1.

Looking at (3.9) again we can say that all points on the I axis are steady states and these are the only ones, so $I(\pm\infty) = 0$. Using (3.12), and the fact that its values at $t = \pm\infty$ must

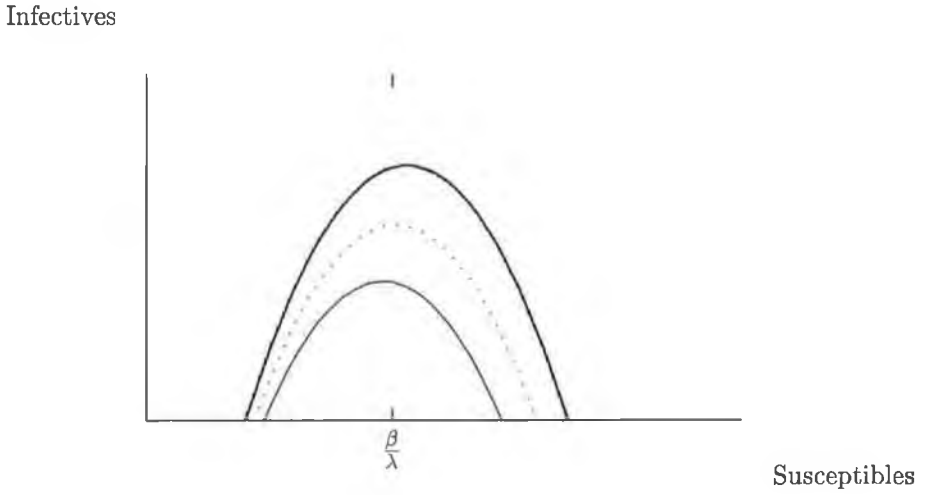

Figure 3.1: Orbits of (3.9)

be equal, we can say

$$\frac{\beta}{\lambda}\ln S(+\infty) - S(+\infty) \;=\; \frac{\beta}{\lambda}\ln N - N \tag{3.14}$$

and we can rewrite (3.14) as

$$\ln\frac{S(+\infty)}{N} \;=\; \frac{\lambda N}{\beta}\Big(\frac{S(+\infty)}{N} - 1\Big). \tag{3.15}$$

We let $s = S/N$ denote the proportion s of susceptibles S in the total population. We define $s(\infty)$ to be the proportion of susceptibles at the end of an outbreak. Hence we have $1 - s(\infty)$ to be the *final size*, $s(\infty)$ is a root of (3.15). We can then rewrite (3.14) as

$$\ln s(\infty) \;=\; R_0\Big(s(\infty) - 1\Big) \tag{3.16}$$

and we define (3.16) as the *final size equation.* Here we define the *final size* to be the fraction of remaining susceptibles in the population after an outbreak has occurred. The *final size* depends on the reproduction ratio, R_0 of the infection and the initial number of susceptibles in the population.

When, $R_0 < 1$ the root is $s(\infty) = 1$, which means that the introduction of an infective into the population does not lead to a major outbreak. When $R_0 > 1$ there exists a unique root in $(0, 1)$, (the root $s(\infty) = 1$ persists, but becomes redundant). We conclude that a certain fraction, $s(\infty)$, avoid infection with the disease, and $s(\infty)$ is completely determined by R_0 via (3.16) (the larger the value of R_0 the smaller $s(\infty)$ will be) [22].

We can also calculate the value of S for which the epidemic reaches its peak. A necessary condition for this is for I to be maximal, (i.e. $dI/dt = 0$, $d^2I/dt^2 < 0$, which is true). As

$$\frac{dS}{dt} = (\lambda S - \beta)I \tag{3.17}$$

and $I \neq 0$, we can say that for I to be maximal we need $S = \beta/\lambda$, which holds with the *threshold density* in (3.8).

The root $s(\infty)$ of (3.16) is a decreasing function of R_0. Using (3.2) we can say that R_0 is an increasing function of N. Hence we can say that the root $s(\infty)$ becomes smaller when N increases. This is essentially an *overshoot phenomenon*, i.e. there will be many new cases after size of S has dropped below N_T, because there are many infectives in the population.

From the results above we can draw the following conclusions:

- An epidemic will occur only if the number of susceptibles in the population exceeds the threshold density.
- The spread of a disease does not stop when $S = 0$, but when $I = 0$.

Using all of the information above we can now prove the famous Threshold Theorem of epidemiology, which was first proved in 1927 by Kermack and McKendrick [46]. This states that if the number of susceptibles S_0 is initially greater than, but close to, the threshold density, we can estimate the number of individuals that ultimately become infective. Specifically, if $S_0 - N_T$ is small compared to N_T, then the number of individuals who become infective is approximately $2(S_0 - N_T)$.

Theorem 3.1 *Let $S_0 = N_T + \nu_1$ and assume that ν_1/N_T is very small compared to one. Assume, that the initial number of infectives, I_0, is very small. Then the number of individuals that ultimately become infective is $2\nu_1$.*

Biocorollary 3.1:
When a disease is introduced into the population the level of susceptibles is reduced to a point as far below the threshold density as it originally was above it.

proof:

Letting t approach infinity in (3.13) gives

$$0 = I_0 + S_0 - S_\infty + N_T \ln \frac{S_\infty}{S_0}. \tag{3.18}$$

If I_0 is very small compared to S_0 we can neglect it, and (3.18) becomes,

$$\begin{aligned} 0 &= S_0 - S_\infty + N_T \ln \frac{S_\infty}{S_0} \\ &= S_0 - S_\infty + N_T \ln \Big[\frac{S_0 - (S_0 - S_\infty)}{S_0} \Big] \\ &= S_0 - S_\infty + N_T \ln \Big[1 - \Big(\frac{S_0 - S_\infty}{S_0} \Big) \Big]. \end{aligned} \tag{3.19}$$

Now, if $S_0 - N_T$ is small when compared with N_T, then $S_0 - S_\infty$ will be small compared to S_0. Consequently, we can truncate the logarithm part of (3.19) using the Taylor series.

$$\ln \Big[1 - \Big(\frac{S_0 - S_\infty}{S_0} \Big) \Big] = -\Big(\frac{S_0 - S_\infty}{S_0} \Big) - \frac{1}{2} \Big(\frac{S_0 - S_\infty}{S_0} \Big)^2 + \ldots \tag{3.20}$$

after two terms. Then (3.19) becomes

$$\begin{aligned} 0 &= S_0 - S_\infty - N_T \Big(\frac{S_0 - S_\infty}{S_0} \Big) - \frac{N_T}{2} \Big(\frac{S_0 - S_\infty}{S_0} \Big)^2 \\ &= (S_0 - S_\infty) \Big[1 - \frac{N_T}{S_0} - \frac{N_T}{2{S_0}^2} (S_0 - S_\infty) \Big]. \end{aligned} \tag{3.21}$$

Solving for $(S_0 - S_\infty)$, we see that

$$\begin{aligned} S_0 - S_\infty &= 2S_0 \Big(\frac{S_0}{N_T} - 1 \Big) \\ &= 2(N_T + \nu_1) \Big[\frac{N_T + \nu_1}{N_T} - 1 \Big] \\ &= 2(N_T + \nu_1) \frac{\nu_1}{N_T} \\ &= 2N_T \Big(1 + \frac{\nu_1}{N_T} \Big) \frac{\nu_1}{N_T} \\ &\cong 2\nu_1. \end{aligned}$$

◇

Throughout the course of an epidemic it is extremely difficult to accurately ascertain the number of new infectives being produced each day or week. Usually the number of infectives is not recorded, but the number of removals are. So, in order to be able to compare the model in (3.1) with that of data from an actual epidemic, we must find the quantity dR/dt as a function of time. From (3.1) and using the fact that $S + I + R = N$, we can say

$$\frac{d}{dt} R(t) = \beta(N - S - R) \tag{3.22}$$

and also observe that

$$\frac{dS}{dR} = \frac{-\lambda S}{\beta}. \tag{3.23}$$

Solving (3.23) and putting into (3.22) we get

$$\frac{d}{dt}R(t) = \beta(N - S_0 \exp^{-\beta R/\lambda} - R). \tag{3.24}$$

After some algebraic calculations involving the Taylor series and the hyberbolic tangent function, we can write (3.24) as

$$\frac{d}{dt}R(t) = \frac{\beta\epsilon^2}{2S_0}\operatorname{sech}^2\left(\frac{\epsilon\beta t}{2} - \tau\right) \tag{3.25}$$

where

$$\epsilon = \left(\frac{\beta}{\lambda}\right)^2\left[\left(\frac{\beta S_0}{\lambda} - 1\right)^2 + \frac{2\beta^2 S_0(N - S_0)}{\lambda^2}\right]^{1/2}$$

and

$$\tau = \tanh^{-1}\frac{1}{\epsilon}\left(\frac{\lambda S_0}{\beta} - 1\right).$$

Equation (3.25) is defined as the epidemic curve of the disease [46], and is shown in Figure 3.2. It illustrates the common observation that in an actual epidemic, the number of infectives climbs to a peak value and then begins to fall away.

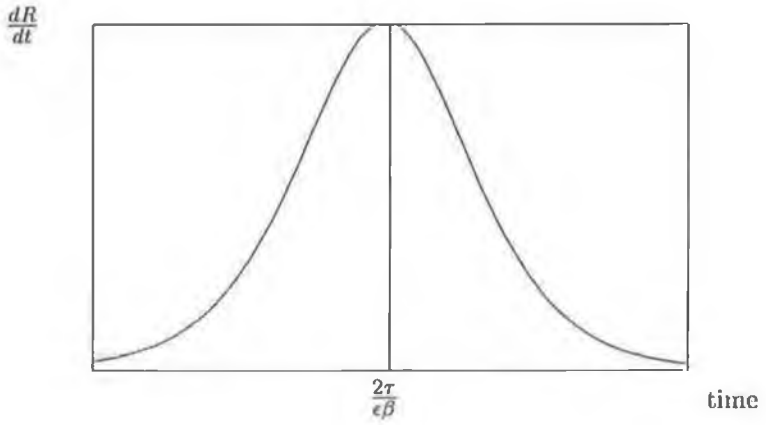

Figure 3.2: Epidemic curve of the disease

3.2 AD Model

As mentioned in Chapter 1, AD can be classed as an SIL model. Unfortunately, SIL models are more difficult to work with than SIR models. This is because there is a continuous flow from the infectives to the latents and vice versa. Also, there is no R term, so it is possible for the disease to remain in the population for a considerable time. For convenience, we rewrite here the equations of Hethcote's model that was mentioned in Chapter 1. For ease of notation we write $d(\cdot)/dt$ as $(\cdot)'$ and $(\cdot)(t)$ as $(\cdot)$

$$S'(t) = -\lambda IS + (\delta_1 + \alpha_1) - (\delta_1 + \alpha_1)S - \alpha_1 I \tag{3.26a}$$

$$I'(t) = \lambda IS - \gamma_1 I - \delta_1 I \tag{3.26b}$$

$$R'(t) = 1 - S(t) - I(t). \tag{3.26c}$$

From (3.26) we create our model for AD. The main differences between (3.26) and our model are the additional L and P terms and the harvesting parameter, mentioned in Chapter 1. We take our model of AD to be:

$$S'(t) = \alpha N - \lambda \frac{I_N S}{N} - (\mu + E)S - \kappa S \tag{3.27a}$$

$$I_N{}'(t) = \lambda \frac{I_N S}{N} - (\mu + E)I_N - \beta I_N + \delta L \tag{3.27b}$$

$$I_V{}'(t) = \lambda_V \frac{I_V P}{N} - (\mu + E)I_V - \eta I_V + \gamma L \tag{3.27c}$$

$$L'(t) = -\gamma L + \eta I_V - (\mu + E)L + \beta I_N - \delta L \tag{3.27d}$$

$$P'(t) = \kappa S - (\mu + E)P - \lambda_V \frac{I_V P}{N} \tag{3.27e}$$

where we define the following parameters

λ = the daily contact rate between individuals

λ_V = average level of protection

α = the birth rate

μ = the death rate

E = the harvesting rate

β, η = the rate of relapse from I_N, I_V respectively

δ, γ = the reactivation rate from I_N, I_V respectively

κ = the vaccination rate

I_N = where infection occurs from a *non-vaccinated* animal

I_V = where infection occurs from a *vaccinated* animal

We take a compartment model of ADV to be and the new term

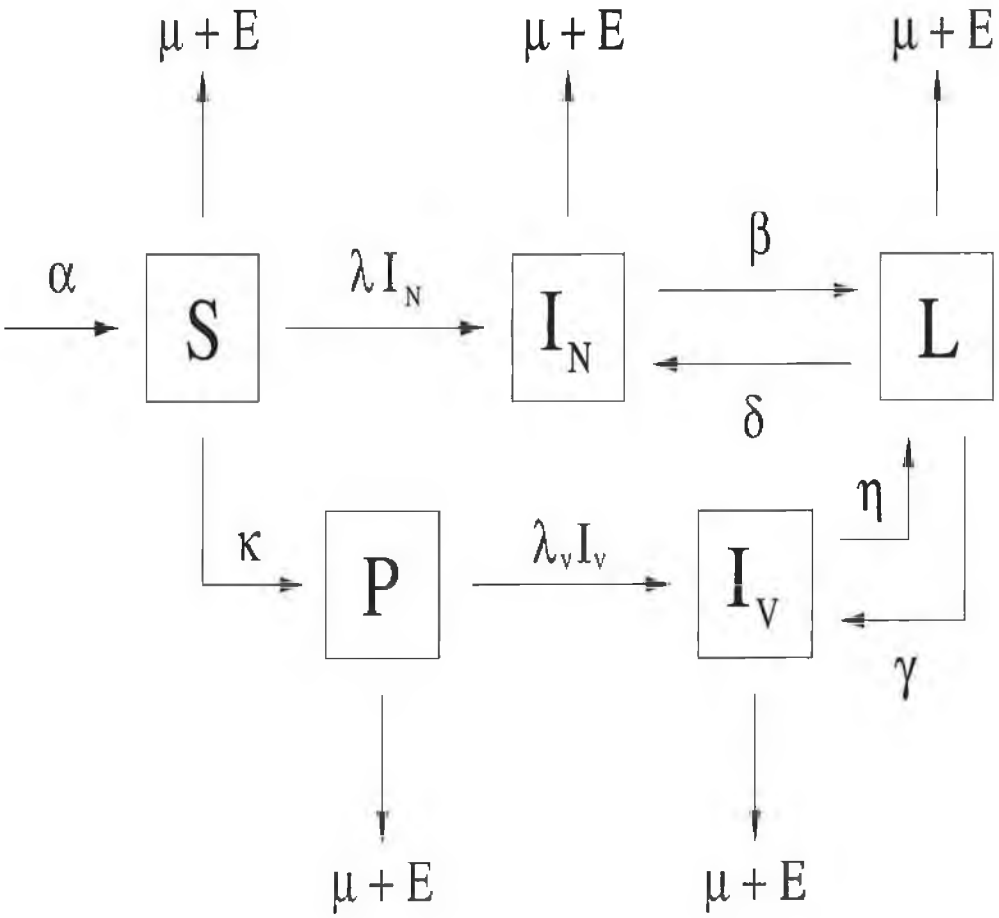

Figure 3.3: Compartment model of AD

P = the number of protecteds in the population (i.e. animals who have been vaccinated against AD and for a while are unable to become infective)

As before

$$S + I + L + P = N.$$

3.2.1 Model Assumptions

The model defined in (3.27) is NOT a coupled model, but instead it incorporates two separate models, *non-vaccinated* and *vaccinated*. This is done to make the model more realistic, as we assume that the farmer is either vaccinating or not (it does not make economic sense to begin a vaccination scheme and not complete it). Hence, for example, a transmission from $I_V \to L \to I_N$ is not possible. We will work with both models, but later on we will just concentrate on the *vaccinated* model as we believe that the majority of the larger producers are vaccinating [44].

The environmental capacity of AD is ignored. This is where the disease is transmitted between a herd from animals other than swine. As mentioned in Chapter 1, this is a problem in mainland Europe, where antibodies have been detected in wild boar [84], and also in the USA, where raccoons are believed to be carriers of the disease [92]. There are no wild boar in Ireland, and the threat of infection from raccoons is unlikely. Also, as most farms are intensive pig producing units, this threat can be ignored.

As mentioned in Chapter 1, the population considered has constant size N which is sufficiently large so that the sizes of each class can be considered as continuous variables instead of discrete ones. As a result we can say that births equal deaths plus harvesting ($\alpha = \mu + E$) (this constraint will be relaxed later in Chapter 5). As farmers work on an all in - all out basis, this is not an unrealistic assumption. Individuals are removed by death from each class at a rate proportional to the class size with proportionality constant μ, which is called the daily death removal rate. The average lifetime is $1/(\mu + E)$.

If the model is to include vital dynamics, then it is assumed that births *and* deaths from natural causes and slaughtering occur. We also assume that there are no deaths from ADV, which is based on previous work done by [72]. We make the important assumption that all newborns are born protected due to maternal antibodies. Hence, the αN term is in S only. However, these antibodies do not last for very long and the piglets are usually vaccinated in weeks 10 and 14 after birth [13].

The population is uniform and homogeneously mixing. This means that every pig has an

equal chance of meeting every other pig that are housed in their particular compartment. The daily contact rate λ is the average number of contacts per infective per day. Thus the *incidence* (number of new cases per unit time) is $\lambda IS/N$. We also define $\lambda_i = \lambda I/N$ to be the *force of infection*, i.e. the average number of contacts with infectives per unit time.

A contact of an infective is an interaction, which results in infection of the other individual if they are susceptible. The daily contact rate λ is fixed and does not vary seasonally, as it does with other diseases [2]. We use the 'true mass action' transmission terms $\lambda IS/N$ and $\lambda IP/N$, rather than the 'classical mass action' transmission term λIS. It has been argued that the former is more accurate than the latter [28], [57].

The incubation period for ADV is usually one week and sometimes less [36]. Hence our model has a latent period *after* infection as opposed to other diseases where the latent period occurs *before* infection. This is contrary to the usual terminology in epidemiology, in which the latent period is the time from infection until the individual becomes infectious [25], but as ADV has the ability to remain in the pig for life, we feel that our latent period after infection is more appropriate.

To begin with, the latent period is zero, i.e. we are assuming the disease is starting in a herd for the first time and therefore there will be no resurgence of the disease from previous infection. Vaccination is usually three times a year depending on the type of pigs that are vaccinated [84]. For example, piglets are vaccinated and age 10 and 14 weeks, while fattening herds are usually double vaccinated [76]. In comparison with single vaccination, double vaccination significantly reduces the risk if extensive virus spread [74], [76]. Antibody titres are usually not measured, i.e. the loss of immunity in the herd is not taken into account.

The vaccination rate is a very important aspect of the *vaccinated* model given the fact that vaccination does not give life long immunity as it does with other diseases. Hence we will have to take re-vaccination and loss of immunity into account. This will be looked at in more detail in Section 3.5.3.

3.3 Reproduction Ratio

The reproduction ratio was first discussed in Section 3.1. Now we discuss in more detail one of the most important parameters used in disease modelling. We observe that secondary infections are produced at a certain rate throughout the lifetime of the infectious individual. Of these, a fraction will return from the latent period to become the second generation of infectious individuals. We therefore define, R_0, the reproduction ratio, to be:

$$\frac{\text{number of secondary infections} \times \text{expected lifetime of infectives}}{\text{the expected survivors of the latent period}}$$

Note:

The reproduction ratio that we discuss in this section is not the same as the reproduction rate, that was discuss in great detail in [2] and [7]. The following work on the reproduction ratio is in line with the more recent work in [19] and [22].

The reproduction ratio can provide significant insight into the transmission dynamics of a disease and can guide strategies to control its spread [35]. For our model of AD we have R_N which represents the reproduction ratio for *non-vaccinated* and R_V which represents the *vaccinated* population. We would expect $R_N > R_V$ according to the definition of the systems. Much work has been done on R_0 in recent years [2], [19].

3.3.1 Calculation of R_N, R_V

We can calculate R_N using the equations in (3.27) and the formula in Diekmann [22]

$$R_0 = \lambda \int_0^\infty \mathcal{A}(\omega) d\omega \tag{3.28}$$

where

$$\mathcal{A}(\omega) = \begin{cases} p \text{ if } T_1 < \omega < T_2 \\ 0 \text{ otherwise}. \end{cases}$$

In words $\mathcal{A}(\omega)$ is the expected infectivity at time ω after infection took place. By infectivity, we mean the probability of transmission given a contact between a susceptible and an infective of disease age ω (ω is the *infection-age* mentioned in Section 3.1).

Because we are interested in the total number of individuals infected by one infectious individual during its total infectious period [85], the infectivity $\mathcal{A}(\omega)$ can be calculated from the following equations

$$I' = -\alpha I - \beta I + \delta L \tag{3.29a}$$

$$L' = -\alpha L + \beta I - \delta L \tag{3.29b}$$

so that $I(0) = 1, L(0) = 0$.

From (3.29a), we can write L in terms of I

$$L = \frac{1}{\delta}\Big(I' + (\alpha + \beta I\Big). \tag{3.30}$$

Putting (3.30) into (3.29b) gives

$$\frac{d}{dt}\left(\frac{1}{\delta}\Big(I' + (\alpha + \beta I\Big)\right)' = \beta I - (\alpha + \delta)\frac{1}{\delta}\Big(I' + (\alpha + \beta I\Big) \tag{3.31}$$

and we can simplify (3.31) to

$$I'' + (2\alpha + \beta + \delta)I' + \alpha(\alpha + \beta + \delta)I = 0. \tag{3.32}$$

The general solution of (3.32), from [14], is

$$I'(t) = C_1 e^{-\alpha t} + C_2 e^{-(\alpha+\beta+\delta)t}. \tag{3.33}$$

The next thing that we need to do is to find C_1 and C_2 for $t = 0$ and $I(0) = 1$, $L(0) = 0$. From (3.33) we can say $C_1 + C_2 = 1$. Putting this information into (3.30) gives

$$\frac{1}{\delta}\Big(I'(0) + (\alpha + \beta)\Big) = 0 \tag{3.34}$$

which holds when $I'(0) = -(\alpha + \beta)$.

Differentiating (3.33) gives

$$\frac{d}{dt}I' = -\alpha C_1 e^{-\alpha t} - (\alpha + \beta + \delta)C_2 e^{-(\alpha+\beta+\delta)t}. \tag{3.35}$$

Putting $I'(0) = -(\alpha + \beta)$ into (3.35) gives

$$-(\alpha + \beta) = -\alpha C_1 - (\alpha + \beta + \delta)C_2$$

and using the fact that $C_1 + C_2 = 1$, we have

$$C_1 = \frac{\delta}{\beta+\delta}, \quad C_2 = \frac{\beta}{\beta+\delta}.$$

Using (3.28) and (3.33) we can say

$$\begin{aligned} R_N &= \lambda \int_0^\infty \left(\frac{\delta}{\beta+\delta} e^{-\alpha t} + \frac{\beta}{\beta+\delta} e^{-(\alpha+\beta+\delta)t} \right) dt \\ &= \lambda \left(\frac{\delta}{\beta+\delta} \right) \left[\frac{-1}{\alpha} e^{-\alpha t} \right]_0^\infty + \lambda \left(\frac{\beta}{\beta+\delta} \right) \left[\frac{-1}{\alpha+\beta+\delta} e^{-(\alpha+\beta+\delta)} \right]_0^\infty \\ &= \lambda \left(\frac{\delta}{\beta+\delta} \right) \left(\frac{1}{\alpha} \right) + \lambda \left(\frac{\beta}{\beta+\delta} \right) \left(\frac{1}{\alpha+\beta+\delta} \right) \\ &= \frac{\lambda(\alpha+\delta)}{\alpha(\alpha+\beta+\delta)}. \end{aligned}$$

Hence we can now say

$$R_N = \frac{\lambda(\alpha+\delta)}{\alpha(\alpha+\beta+\delta)}. \tag{3.36}$$

From this we can say that the *critical reactivation rate*, i.e. the reactivation rate for which $R_N \geq 1$, can be calculated as

$$\delta = \frac{\alpha(\alpha+\beta-\lambda)}{\lambda-\alpha}. \tag{3.37}$$

Note:

1. R_N can also be calculated using stability analysis (see Appendix A for further details).

2. If λ is small compared with α, i.e. in model terms, if the contact rate is smaller than the birth rate, R_N will be less than 1 and as a result the disease can be removed more easily from the population. If $\lambda > \alpha + \beta$, $R_N \geq 1$, regardless of δ. We can also say that when

$$\lambda < \frac{\alpha(\alpha+\beta+\delta)}{\alpha+\delta} \iff R_N < 1 \tag{3.38}$$

so small enough λ (regardless of α, β, δ) aids the removal of ADV.

3. R_N does not depend on the size of the population (there is no N term in (3.36)), so the size of the population does not have any bearing on control measures. This is contrary to earlier work in [2], [72], but in line with more recent work in [12], [84].

3.3.2 Further R_0 calculations

It has been shown that when $R_0 < 1$, an infection will fail to spread and will eventually fade out, with only a few infected individuals (this is known as a minor outbreak) [85]. On the other hand, when $R_0 > 1$ the infection will spread, resulting in many infected individuals (major outbreak), or an infection can, by chance, fade out early (i.e. at the earliest stages) resulting in only a few infectives (minor outbreak).

The next thing we do is to determine R_0 at different scales, i.e. at the one end with herds as units and at the other end with compartments as units. We define

$$\begin{aligned} R_{ind} &= \text{the } R_0 \text{ between individuals} \\ R_{herd} &= \text{the } R_0 \text{ between herds} \\ R_{comp} &= \text{the } R_0 \text{ between compartments} \end{aligned}$$

(if $R_{ind} > 1$ the size of the herd is particularly important).

With regard to vaccinating a region, ADV must not be allowed to spread extensively after introduction into a population. This ability to spread is measured by R_{herd}. If $R_{herd} < 1$ very few herds will become infective. On the other hand, if $R_{herd} \geq 1$ many herds may become infective. So ADV can be eradicated from a region when $R_{herd} < 1$.

If we consider that a pig population is made up of units (we use units to determine R_0 at different scales; at one end the region with the herds as units and at the other end compartments with the pigs as units). These units will interact with units in their own group (herd) and with units in other groups. We can estimate R_0 for units within a group, and also for groups. We also need to derive a relationship between R_0 of groups (G_R) and with R_0 of units (U_R) within these groups. This has been done extensively in the Netherlands [84], [85].

We make the following additional assumptions:

- group infected when ≥ 1 units infected

- contact between groups is the number of transmissions of ADV per unit of time of a unit of a group with a unit of a different group (λG_R)
- number of units in a group is constant.

If we return to our original definition of R_0 at the beginning of the section we can now say that R_0 is the product of the susceptibles in a group (G_S), the infectivity of a group (G_I) and the contact rate between groups (λG_R), or in mathematical terms:

$$G_R = (G_S)(G_I)(\lambda G_R)\,. \tag{3.39}$$

The susceptibility of a group (G_S) is the same as the the susceptibility of a unit (g_s) and infectivity of a group (G_I) is the same as infectivity of a unit (g_i) times the average taken over all infectious units (number of infectious units/group) during an outbreak. We call this the *total average*. To calculate the *total average*, minor and major outbreaks are taken into account and the possibility of persistence of infection within the group. Because of persistence, the *total average* number of infectious units can be greater than the total number of units present in the group.

For the contact rate, the herd size must be taken into account, hence λG_R is the contact rate of a group with a unit of another group. When the 'receiving' group has S individuals, λG_R becomes $\lambda S G_R$, so (3.39) becomes

$$G_R = (g_s)(g_i)(\text{number of infectious units/group})(\lambda G_R) \tag{3.40}$$

and we write (3.40) as

$$G_R = (U_R)(\text{number of infectious units/group})\Big(\frac{\lambda G_R}{\lambda U_R}\Big)$$

where U_R is the susceptibilty of a unit times the infectivity of a unit times the contact rate between units. Hence

$$G_R = (U_R)(\text{number of infectious units per group})\mathcal{F}$$

where $\mathcal{F}$ is the relative contact rate of a unit, i.e.

$$\mathcal{F} = \frac{\text{contact rate of a unit with units in a different group}}{\text{contact rate of a unit with units in its own group}}$$

As the transmissions between pigs within herds is greater than transmissions between pigs of separate herds, we can safely say, $\mathcal{F} < 1$. Then we can also say

$$R_{comp} = R_{ind} \text{ (total number of infectious pigs per compartment)}(\mathcal{F})$$

To be able to work out the dynamics within the compartments to a sufficient accuracy a stochastic model is necessary. This will be looked at in Chapter 4.

3.3.3 Threshold Density

The criterion $R_0 > 1$ for an outbreak of the disease can equivalently be expressed as the requirement that the proportion of susceptibles in the population exceeds a certain *threshold density*, $S > N_T$, (where N is the total population) with the definition

$$N_T = \frac{1}{R_N} \tag{3.41}$$

in terms of our model, the threshold density for the *non-vaccinated* model can be written as

$$N_T = \frac{\alpha(\alpha+\beta+\delta)}{\lambda(\alpha+\delta)}. \tag{3.42}$$

This is a very important parameter in our model as when the susceptibles are below N_T, $R_N < 1$ and the chances of an outbreak occurring are very small compared to when the susceptibles are above N_T. However it is still possible for $R_N > 1$ and an outbreak not occurring, but this would be very unfortunate (for the disease).

Following on from this we calculate the *initial exponential growth rate* for the *non-vaccinated* model to be

$$r_N = \lambda N - (\alpha+\beta). \tag{3.43}$$

When N is large in (3.43), the initial growth rate will be quite large. This is what we would expected to happen if an outbreak occurred in a fully susceptible population.

3.4 Non Vaccinated Model

3.4.1 Introduction

From (3.27), dropping the suffix N, we can write the SIL model as

$$S'(t) = \alpha N - \lambda \frac{IS}{N} - (\mu + E)S \tag{3.44a}$$

$$I'(t) = \lambda \frac{IS}{N} - (\mu + E)I - \beta I + \delta L \tag{3.44b}$$

$$L'(t) = \beta I - \delta L - (\mu + E)I\,. \tag{3.44c}$$

For convenience we write these equations in terms of fractions of individuals in each class. Define $s = S/N$, $i = I/N$, $l = L/N$. The equations in (3.44) become

$$s'(t) = \alpha - \lambda is - (\mu + E)s \tag{3.45a}$$

$$i'(t) = \lambda is - (\mu + E)i - \beta i + \delta l \tag{3.45b}$$

$$l'(t) = \beta i - \delta l - (\mu + E)l \tag{3.45c}$$

where

$$s + i + l = 1. \tag{3.46}$$

For computational ease we return to the original notation of S, I and L and we introduce the constant population restriction ($\alpha = \mu + E$). Hence (3.45) becomes

$$S'(t) = \alpha - \lambda IS - \alpha S \tag{3.47a}$$

$$I'(t) = \lambda IS - \alpha I - \beta I + \delta L \tag{3.47b}$$

$$L'(t) = \beta I - \delta L - \alpha L \tag{3.47c}$$

and

$$S + I + L = 1. \tag{3.48}$$

3.4.2 Non Vaccinated Model

We calculate the equilibrium points of (3.47) to be

$$(S^*, I^*, L^*) = (1, 0, 0) \tag{3.49}$$

which we define to be the disease free equilibrium (DFE), and

$$(S^*, I^*, L^*) = \left(\frac{1}{R_N}, \frac{\alpha}{\lambda}(R_N - 1), \frac{\beta}{(\alpha+\delta)}(R_N - 1)\right) \tag{3.50}$$

where

$$R_N = \frac{\lambda(\alpha+\delta)}{\alpha(\alpha+\beta+\delta)}$$

and we define (3.50) as the disease present equilibrium (DPE).

At the DPE the *force of infection*, first mentioned in Section 3.2.1, satisfies the equation

$$\lambda_i = \alpha(R_N - 1) \tag{3.51}$$

so that there is a positive *force of infection* when $R_N > 1$.

Theorem 3.4.1 *The DFE (3.49) always exists. (1) This equilibrium is asymptotically stable when $R_N < 1$ and unstable when $R_N > 1$. (2) When the DPE (3.50) exists, i.e. for $R_N > 1$, it is asymptotically stable when $R_N > 1$.*

Biocorollary 3.4.1:
If the reproduction ratio exceeds one, all solutions (except the DFE) will approach the DPE and the disease will remain endemic in the population. Hence, the susceptible fraction decreases as the infective fraction increases, and eventually the entire population will become infected. If the reproduction ratio is less than one, all solutions approach the DFE, at which they will remain. Hence, the susceptible fraction increases as the infective fraction decreases to zero, and eventually the entire population will become susceptible. When the reproduction ratio equals one, only the DFE exists.

First we linearise the equations in (3.47), this is done using

$$S_1 = S - S^*, \;\; I_1 = I - I^*, \;\; L_1 = L - L^*$$
$$\Rightarrow S = S_1 + S^*, \;\; I = I_1 + I^*, \;\; L = L_1 + L^*$$

where (S^*, I^*, L^*) are the equilibrium points. We can write (3.47) as

$$S'(t) = \alpha - \lambda(I_1 + I^*)(S_1 + S^*) - \alpha(S_1 + S^*) \tag{3.52a}$$
$$I'(t) = \lambda(I_1 + I^*)(S_1 + S^*) - (\alpha + \beta)(I_1 + I^*) + \delta(L_1 + L^*) \tag{3.52b}$$
$$L'(t) = \beta(I_1 + I^*) - \delta(L_1 + L^*) - \alpha(L_1 + L^*) \tag{3.52c}$$

Observe that, by definition of the equilibrium states, $\alpha - \lambda I^* S^* - \alpha S^* = 0$, $\lambda I^* S^* - (\alpha + \beta) I^* + \delta L^* = 0$, $\beta I^* - \delta L^* - \alpha L^* = 0$, which cancels out the apparent non-homogeneous term in (3.52). Ignoring the non linear terms and dropping the suffix one, we calculate the linearised matrix of (3.47) to be:

$$\begin{pmatrix} S \\ I \\ L \end{pmatrix}' = \begin{pmatrix} -(\alpha + \lambda I^*) & -\lambda S^* & 0 \\ \lambda I^* & \lambda S^* - (\alpha + \beta) & \delta \\ 0 & \beta & -(\alpha + \delta) \end{pmatrix} \begin{pmatrix} S \\ I \\ L \end{pmatrix}. \tag{3.53}$$

Proof of Theorem (3.4.1):

(1) Putting the DFE in (3.49) into (3.53) we get

$$\begin{pmatrix} -\alpha & -\lambda & 0 \\ 0 & \lambda - (\alpha + \beta) & \delta \\ 0 & \beta & -(\alpha + \delta) \end{pmatrix} \tag{3.54}$$

Next we let (3.54) be $\mathbf{A}$. Now we need to find the solutions of

$$det(\mathbf{A} - \rho I) = 0 \tag{3.55}$$

for the eigenvalues ρ of $\mathbf{A}$. This is known as the characteristic equation, and we calculate it to be

$$\rho^3 + a_1\rho^2 + a_2\rho + a_3 = 0 \tag{3.56}$$

where

$$a_1 = 2\alpha + \lambda\Big(\frac{1}{R_N} - 1\Big) + \frac{\delta\lambda}{\alpha R_N}$$

$$a_2 = \lambda(\alpha+\delta)\Big(\frac{2}{R_N} - 1\Big) + \alpha(\alpha - \lambda)$$

$$a_3 = \alpha\lambda(\alpha+\delta)\Big(\frac{1}{R_N} - 1\Big)$$

where R_N is as before.

We can use the Routh-Hurwitz test [80] to determine the stability of (3.56) without having to solve the equation. This says that given

$$c(\rho) = \rho^n + a_1\rho^{n-1} + \ldots + a_n = 0$$

the $\mathrm{Re}(\rho_i) < 0 \ \forall \ i$, if the principal minors $\Delta_1, \Delta_2, \ldots, \Delta_n$ are all positive, where

$$\Delta_1 = a_1, \quad \Delta_2 = \begin{vmatrix} a_1 & 1 \\ a_3 & a_2 \end{vmatrix}, \ldots$$

Note that $a_m = 0 \ \forall \ m > n$ in the construction of Δ_i above, $\forall \ i$. Applying the Routh-Hurwitz test we have $\Delta_1 = a_1$, $\Delta_2 = a_1.a_2 - a_3$ and $\Delta_3 = a_3(a_1.a_2 - a_3)$.

If $R_N < 1$:

If $R_N < 1$ we can show that $a_1, a_3 > 0$, hence $\Delta_1 > 0$. For $a_2 > 0$ we need

$$\lambda(\alpha+\delta)\Lambda_1 > \alpha(\lambda - \alpha) \tag{3.57}$$

where

$$\Lambda_1 = \frac{2}{R_N} - 1\,.$$

We know that $\Lambda_1 > 1$, as $R_N < 1$, so we can say that $\alpha\lambda\Lambda_1 > \alpha\lambda$. The right hand side of (3.57) is less that $\alpha\lambda$, as all parameters are positive, so we can say that

$$\alpha\lambda\Lambda_1 > \alpha(\lambda - \alpha)\,. \tag{3.58}$$

Hence (3.57) is true, hence $a_2 > 0$. For Δ_2, $\Delta_3 > 0$, we need to look at whether or not $a_1.a_2 > a_3$, i.e.

$$\Big(2\alpha + \lambda\Lambda_2 + \frac{\lambda\delta}{\alpha R_N}\Big)\Big(\lambda(\alpha+\delta)\Lambda_1 + \alpha(\alpha - \lambda\Big) > \alpha\lambda(\alpha+\delta)\Lambda_2 \tag{3.59}$$

where Λ_1 is as before, and

$$\Lambda_2 = \frac{1}{R_N} - 1 .$$

We know a_1, a_2, $a_3 > 0$. Since $R_N < 1$, we always have $\Lambda_1, \Lambda_2 > 1$ and $\Lambda_1 > \Lambda_2$, hence we can say that

$$2\alpha\lambda(\alpha+\delta)\Lambda_1 > \alpha\lambda(\alpha+\delta)\Lambda_2 . \tag{3.60}$$

If the remaining terms on the left hand side of (3.59) are nonnegative we can say that (3.59) is true, i.e, we need

$$\Big(2\alpha^2 + \alpha\lambda\Lambda_2 + \frac{\delta\lambda}{R_N}\Big)(\alpha-\lambda) + \lambda^2(\alpha+\delta)\Lambda_1\Big(\Lambda_2 + \frac{\delta}{\alpha R_N}\Big) > 0 \tag{3.61}$$

and we can write (3.61) as

$$\alpha^2(2\alpha + \lambda\Lambda_2 - 2\lambda) + \lambda^2\Lambda_2(\Lambda_3 - \alpha) + \frac{\lambda\delta}{\alpha R_N}\Big(\alpha^2 + \lambda\Lambda_3 - \alpha\lambda\Big) > 0 \tag{3.62}$$

where $\Lambda_3 = (\alpha+\delta)\Lambda_1$. We know $\Lambda_1, \Lambda_2 > 1$ and we can see that all terms on the left hand side of (3.62) are positive. Hence (3.62) is true.

It follows that (3.61) is true, and from this we can say that (3.59) is also true.

$$\Rightarrow \Delta_i > 0 \ \forall \ i \in [1,3]$$
$$\Rightarrow Re(\rho_i) < 0$$

Using Theorem A.1.2 we can show that ρ_i are asymptotically stable when they are < 0. Hence the DFE (3.49) is asymptotically stable when $R_N < 1$.

If $\mathbf{R_N > 1}$:

If $R_N > 1$, we can show that $a_1 > 0$ and $a_3 < 0$. Thus $\Delta_1 > 0$. Now $\Delta_3 = a_3.\Delta_2$. If $\Delta_2 > 0$, then $\Delta_3 < 0$, and unstable, while if $\Delta_2 < 0$, then $\Delta_3 > 0$, so again unstable. Hence, using the converse of the Routh-Hurwitz test, we can say that not all principal minors are positive, hence not all eigenvalues have negative real part.

As one eigenvalue is positive we can use Theorem A.1.2, to say that the DFE (3.49) is unstable when $R_N > 1$.

(2) Next we put the DPE in (3.50) into (3.53) to give

$$\begin{pmatrix} -\alpha R_N & \frac{\lambda}{R_N} & 0 \\ \alpha\lambda(R_N-1) & \frac{\lambda}{R_N}-(\alpha+\beta) & \delta \\ 0 & \beta & -(\alpha+\delta) \end{pmatrix} \tag{3.63}$$

As before we find the characteristic equation and this time we calculate it to be

$$\rho^3 + b_1\rho^2 + b_2\rho + b_3 = 0 \tag{3.64}$$

where

$$\begin{aligned} b_1 &= \frac{\delta\lambda}{\alpha R_N} + \alpha(R_N+1) \\ b_2 &= \alpha\lambda\Big(1-\frac{1}{R_N}\Big) + \delta\lambda + \alpha^2 R_N \\ b_3 &= \alpha\lambda(\alpha+\delta)\Big(1-\frac{1}{R_N}\Big) \end{aligned}$$

Again using the Routh-Hurwitz test we have $\Delta_1 = b_1$, $\Delta_2 = b_1.b_2 - b_3$ and $\Delta_3 = b_3(b_1.b_2 - b_3)$.

If $\mathbf{R_N < 1}$:

If $R_N < 1$, then $b_1 > 0$ and $b_3 < 0$. Using the same argument as that for the DFE when $R_N > 1$ we can say that not all eigenvalues have negative real part. We know that $\Delta_3 = b_3\Delta_2$, and as before, when $\Delta_2 > 0$, $\Delta_3 < 0$ and vice versa. Hence, using the converse of the Routh-Hurwitz test, we can say that not all principal minors are positive, hence not all eigenvalues have negative real part.

As one eigenvalue is positive we can use Theorem A.1.2, to say that the DPE (3.50) is unstable when $R_N < 1$.

If $\mathbf{R_N > 1}$:

If $R_N > 1$, then b_1, b_2, $b_3 > 0$. Hence $\Delta_1 > 0$. For Δ_2,$\Delta_3 > 0$ we need $b_1.b_2 > b_3$, i.e.

$$\Big(\frac{\delta\lambda}{\alpha R_N} + \alpha(R_N+1)\Big)\Big(\alpha\lambda\Lambda_3 + \delta\lambda + \alpha^2 R_N\Big) > \alpha\lambda(\alpha+\delta)\Lambda_3 \tag{3.65}$$

where

$$\Lambda_3 \;=\; 1-\frac{1}{R_N}.$$

We know $b_1,\ b_2,\ b_3 > 0$. Expanding the left hand side of (3.65) and just writing the Λ_3 terms, we have

$$\alpha^2\lambda(R_N+1)\Lambda_3 \;>\; \alpha\lambda(\alpha+\delta)\Lambda_3\,. \tag{3.66}$$

Using $\alpha > \delta$, and $R_N > 1$, we can say that

$$\alpha(R_N+1) > \alpha+\delta \tag{3.67}$$

Hence (3.66) is true. As all other terms on the left hand side of (3.65) are positive we can say that this is also true.

$$\begin{aligned} &\Rightarrow \Delta_i \;>\; 0 \;\;\forall\;\; i \;\in\; [1,3] \\ \Rightarrow\; &Re(\rho_i) \;<\; 0 \;\;\forall\;\; i \end{aligned}$$

Using Theorem A.1.2 we can show that ρ_i are asymptotically stable when they are < 0. Hence, the DPE (3.50) is asymptotically stable when $R_N > 1$. ◇

3.4.3 Non Vaccinated Graphs

Over the next few pages we draw some graphs for the *non-vaccinated* model that we have discussed. These graphs are done using Mathematica and the data used in them was taken from ongoing work in the Netherlands [84], and a recent Irish Pig Herd report [55]. However, not all of out parameters have been catered for, so some of them, such as the relapse rate (δ) had to be estimated using previous work done on AD in the USA [71].

We look at graphs at various stages of an epidemic, ranging from just beginning ($I \approx 0, L = 0$), to the middle of an outbreak ($I, L > S$). We also look at what happens to S, I and L when $R_N > 1$ and for $R_N < 1$, to see if Theorem 3.4.1 holds. The initial population has size $N = 100$, and the majority of the graphs are run from between 7 and 30 days. In the following graphs, the red lines represent susceptibles, the green lines represent infectives, and the blue lines represent the latents.

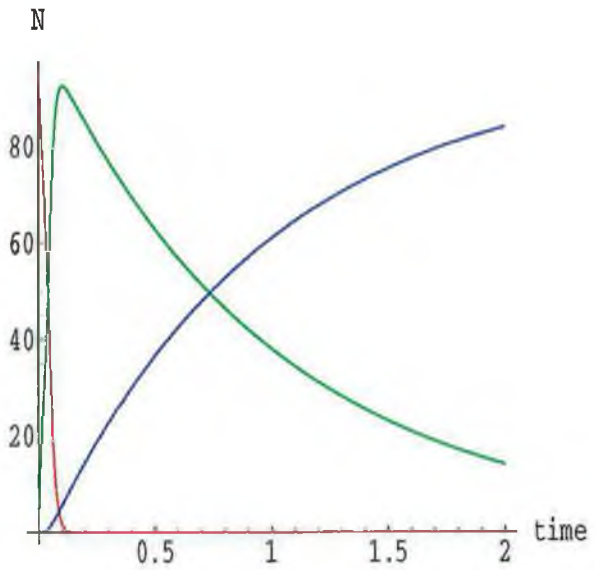

Figure 3.4: Non vaccinated Van Nes model

In the graph above we have used the data from [85] as this is the most recent data that we have to work with. If the graph is to continue for longer, all the population will eventually enter the L compartment. Here $R_N < 1$.

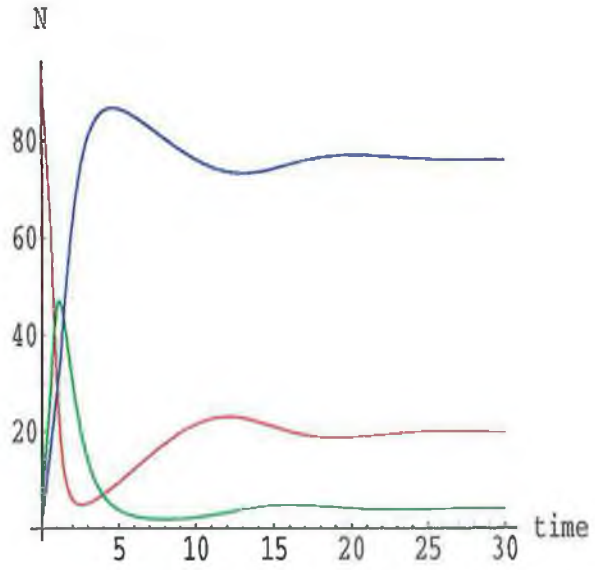

Figure 3.5: Non vaccinated Van Nes model (modified)

Here, we have a similar graph to the one in Figure 3.4, but we have modified the data to suit Irish herds (using [55]) as opposed to Dutch herds, again $R_N < 1$.

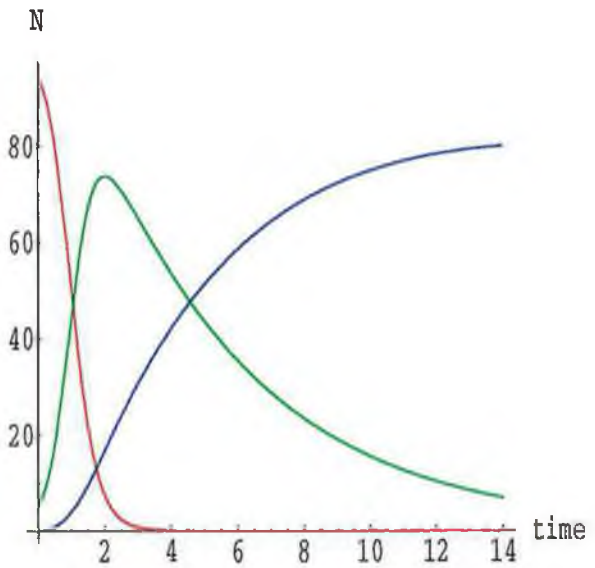

Figure 3.6: Non vaccinated Smith and Grenfell model ($\beta > \delta$)

Here we have used data similar to that used in [71]. We have modified it slightly to make the graph more readable. Again, $S, I \to 0$ and $L \to 1$, and we have $R_N < 1$.

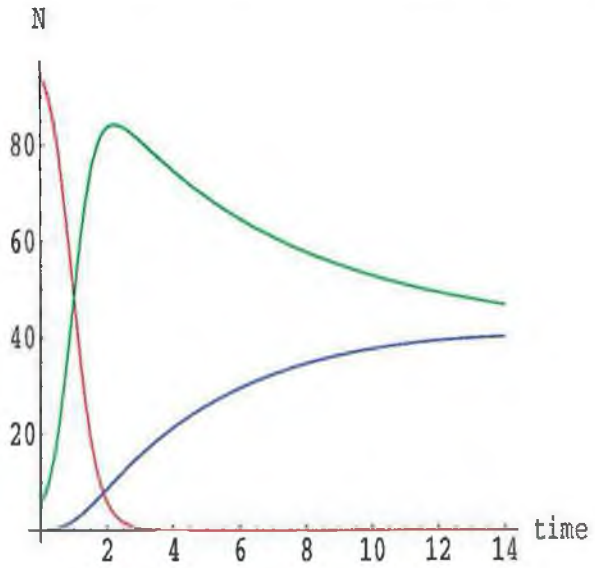

Figure 3.7: Non vaccinated Smith and Grenfell model ($\beta = \delta$)

Here we have adjusted the parameters in Figure 3.6 so that $\beta = \delta$, whereas earlier, we had $\beta > \delta$. This time $S \to 0$, $I, L \to 0.5$ of population, and as expected $R_N > 1$.

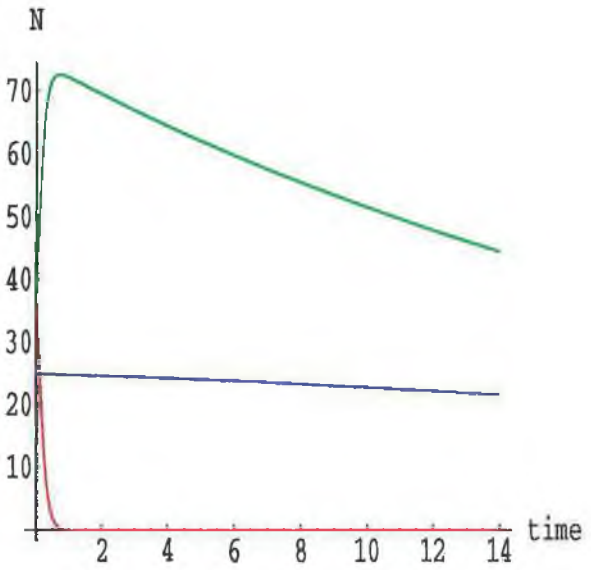

Figure 3.8: Non vaccinated model (epidemic)

In the graph above, we have replaced α with α_w (weekly), where, $\alpha_w = (1+\alpha)^{1/52} - 1$. We have adjusted the other parameters to suit, and $R_N \gg 1$, $S \to 0$, and $I, L \to 0.5$, eventually.

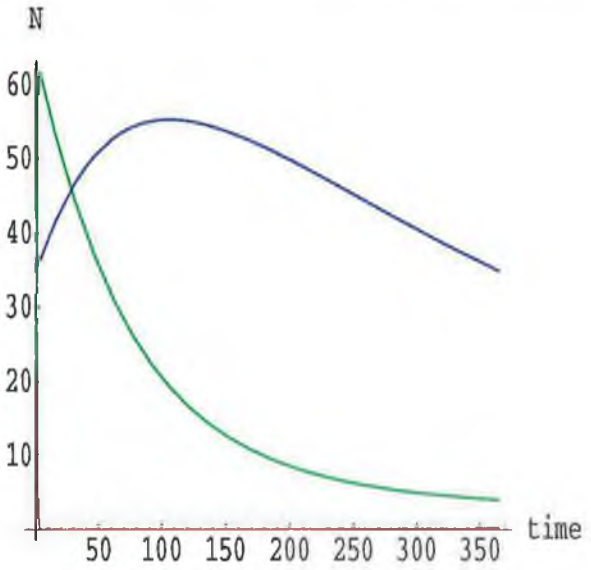

Figure 3.9: Non vaccinated model (long epidemic)

Here we have similar data to that of Figure 3.9, but we have run the graph over longer time (one year), and reduced the β and δ terms. Here $L \to 0.4$, at which the population stays.

3.4.4 Reduced Model

Now we reduce the *non-vaccinated* system in (3.47) to a more workable 2×2 (using 3.46). Hence, we have

$$S'(t) = \alpha - \lambda IS - \alpha S \tag{3.68a}$$

$$I'(t) = \lambda IS - (\alpha + \beta + \delta)I + \delta(1 - S)\,. \tag{3.68b}$$

Here $S(t)$ is the proportion of animals that are susceptible at time t, and $I(t)$ are the proportion of infected animals at time t. For this interpretation to be consistent with the dynamics of (3.68), we must ensure that the forward orbit of every point in

$$\mathcal{T} := (S, I) \in \mathbb{R}^2 : I \geq 0, S \geq 0, S + I \leq 1$$

to be a subset of $\mathcal{T}$. That is, if $\xi = (S, I) \in \mathcal{T}$ we have $\Gamma^+(\xi) \subset \mathcal{T}$.

We calculate the equilibrium points of (3.68) as

$$(S^*, I^*) = F = (1, 0) \tag{3.69}$$

which we define to be the disease free equilibrium (DFE), and

$$(S^*, I^*) = P = \left(\frac{1}{R_N}, \frac{\alpha}{\lambda}(R_N - 1)\right) \tag{3.70}$$

which we define as the disease present equilibrium (DPE) (where R_N is as before).

For $R_N < 1$ we see that only the DFE is contained in $\mathcal{T}$. For $R_N = 1$ the DFE = DPE, while for $R_N > 1$, the DPE is contained in the interior of $\mathcal{T}$. Now we turn to the local asymptotic stability of the DFE and the DPE. Moreover the interior of $\mathcal{T}$ (Int($\mathcal{T}$)) is invariant in finite time.

Lemma 3.4.2 *Let* $\tilde{\mathcal{T}} = \{(S, I) \in \mathbb{R}^2 : I > 0, S > 0, I + S < 1\}$. *Then* $x_0 \in \tilde{\mathcal{T}}$ *implies* $\varphi(t, x_0) \in \tilde{\mathcal{T}}$ *for all* $\infty > t \geq 0$.

Proof:
Suppose that $x_0 \in \tilde{\mathcal{T}}$, and let $t_0 = \inf\{t > 0 : \varphi(t, x_0) \in \mathcal{T} \cap \tilde{\mathcal{T}}\}$. Then $\varphi(t, x_0) = (S(t_0), I(t_0))$ satisfies one of the following:

1. • $I(t_0) = 0, S(t_0) > 0, I(t_0) + S(t_0) < 1$ [1]
   • $I(t_0) = 0, S(t_0) = 0$ [2]
   • $I(t_0) = 0, I(t_0) + S(t_0) = 1$ [?]
2. • $I(t_0) > 0, S(t_0) = 0, I(t_0) + S(t_0) < 1$ [3]
   • $I(t_0) > 0, S(t_0) = 0, I(t_0) = 1$ [3]
3. • $I(t_0) > 0, S(t_0) > 0, I(t_0) + S(t_0) = 1$ [4]

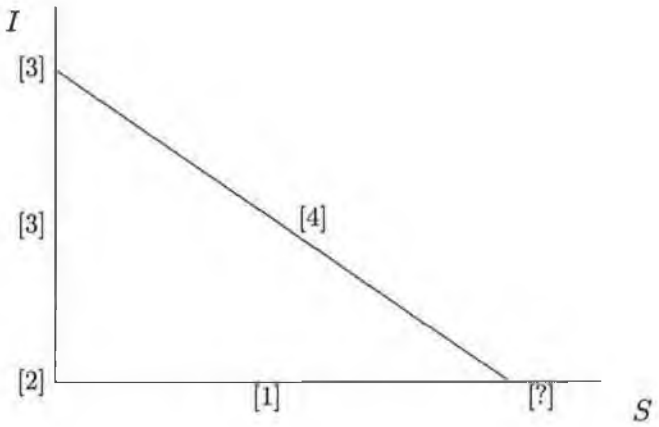

Figure 3.10: Possible outcomes for $\varphi(t, x_0)$

As can be seen in Figure 3.10, in each case, the minimality of time t_0 implies

[1] $I'(t_0) \leq 0$ [2] $S'(t_0) \leq 0$

[3] $S'(t_0) \leq 0$ [4] $I'(t_0) + S'(t_0) \geq 0$.

[1] $I'(t_0) \leq 0$ $[I(t_0) = 0]$

$0 \geq I'(t_0) = \delta(1 - S(t_0)) > 0$ if $0 \leq S(t_0) < 1$, which is a contradiction.

Hence [1] is impossible.

[2] $S'(t_0) \leq 0$ $[S(t_0) = I(t_0) = 0]$

$0 \geq S'(t_0) = \alpha > 0$, which is a contradiction. Hence [2] is impossible.

[3] $S'(t_0) \leq 0$ $[S(t_0) = 0, I(t_0) > 0]$

as in [2], $0 \geq S'(t_0) = \alpha > 0$, which is a contradiction. Hence [3] is impossible.

[4] $I'(t_0) + S'(t_0) \geq 0$

$$\begin{aligned} \frac{d}{dt}\Big[S(t) + I(t)\Big] &= \alpha - \alpha S(t) - \alpha I(t) - \beta I(t) - \delta I(t) + \delta - \delta S(t) \\ &= (\alpha + \delta)(1 - S(t) - I(t)) - \beta I(t) \end{aligned} \tag{3.71}$$

but $0 \leq I'(t_0) + S'(t_0) = -\beta I(t) < 0$, which is a contradiction. Hence [4] is impossible.

[?] $\varphi(t, x_0) = \text{DFE}$,
$x_0 = \varphi(-t_0, \varphi(t, x_0)) = \varphi(-t_0, \text{DFE}) = \text{DFE}$, which is also a contradiction.

Hence there cannot exist $0 < t_0 < \infty$ such that $\varphi(t_0, \underline{x}_0) \notin \tilde{\mathcal{T}}$ whenever $\underline{x}_0 \in \tilde{\mathcal{T}}$. ◇

Lemma 3.4.3 *$\Gamma^+(\xi) \subset \mathcal{T}$ for all $\xi \in \mathcal{T}$.*

Proof:
Can be obtained by following the type of reasoning in Lemma 3.4.2. ◇

Continuing this argument, we see that the boundary of $\mathcal{T}$ cannot be reached, even in infinite time, except for the DFE.

Lemma 3.4.4 *Suppose $x_0 \in \tilde{\mathcal{T}}$. Then $\Gamma^+(x_0) \subset \tilde{\mathcal{T}}$ or $\omega(x_0) = DFE$.*

Proof:
By the above argument $\Gamma^+(x_0) \not\subset \tilde{\mathcal{T}}$, only if

$$\lim_{t \to \infty} \phi(t, x_0) = x_b \in \partial\mathcal{T}. \tag{3.72}$$

Then x_b must be an equilibrium point, viz the DFE and the result follows. To see that x_b satisfying (3.72) is an equilibrium, note for any $S > 0$ that

$$\begin{aligned} \phi(S, x_b) &= \phi\Big(S, \lim_{t \to \infty} \phi(t, x_0)\Big) = \lim_{t \to \infty} \phi\Big(S, \phi(t, x_0)\Big) \\ &= \lim_{t \to \infty} \phi(S + t_0, x_0) = x_b \end{aligned} \tag{3.73}$$

hence x_b is an equilibrium point. ◇

Next we look at the local asymptotic stability (LAS) of both the DFE and the DPE.

Theorem 3.4.5 *1. (i) If $R_N < 1$, then the DFE is a hyperbolic equilibrium. It is, moreover, a stable node.*

(ii) If $R_N > 1$, then the DFE is a saddle.

2. (i) If $R_N < 1$, the the DPE is $\notin \mathcal{T}$.

(ii) If $R_N > 1$, then the DPE is a hyperbolic equilibrium. Moreover, it is a stable equilibrium.

3. If $R_N = 1$, the DFE = DPE, is a unique equilibrium with eigenvalues $0, -\rho^*$, where $\rho^* > 0$

Biocorollary 3.4.5:

If the reproduction ratio exceeds one, all solutions (except the DFE) will approach the DPE and the disease will remain endemic in the population. Hence, the susceptible fraction decreases as the infective fraction increases, and eventually the entire population will become infected. If the reproduction ratio is less than one, all solutions approach the DFE, at which they will remain. Hence, the susceptible fraction increases as the infective fraction decreases to zero, and eventually the entire population will become susceptible.

Proof:

1. (i), (ii) Following on from Theorem (3.4.1) we calculate the linearised matrix of (3.68) to be:

$$\begin{pmatrix} S \\ I \end{pmatrix}' = \begin{pmatrix} -(\alpha + \lambda I^*) & -\lambda S^* \\ \lambda I^* - \delta & \lambda S^* - (\alpha + \beta + \delta) \end{pmatrix} \begin{pmatrix} S \\ I \end{pmatrix} \tag{3.74}$$

Putting the DFE in (3.69) into (3.74) we have

$$J_{DFE} = \frac{\partial(f_1, f_2)}{\partial(x_1, x_2)} = \begin{pmatrix} -\alpha & -\lambda \\ -\delta & \lambda - (\alpha + \beta + \delta) \end{pmatrix} \tag{3.75}$$

We calculate the characteristic equation of (3.75) to be

$$\triangle(\rho) = \rho^2 + c_1\rho + c_2 = 0 \tag{3.76}$$

where

$$\begin{aligned} c_1 &= 2\alpha + \beta + \delta - \lambda \\ c_2 &= \alpha(\alpha + \beta + \delta)(1 - R_N). \end{aligned}$$

1. (ii) is automatic as the product of the eigenvalues of (3.75) is $\rho_1\rho_2 = c_2 < 0$, when $R_N > 1$. Hence (3.75) has a pair of eigenvalues of opposite sign. Suppose $R_N < 1$. Then

$c_2 > 0$, this implies that

$$\lambda \ < \ \frac{\alpha(\alpha+\beta+\delta)}{\alpha+\delta} \tag{3.77}$$

hence

$$\begin{aligned} c_1 &= 2\alpha+\beta+\delta-\lambda \ > \ 2\alpha+\beta+\delta-\frac{\alpha(\alpha+\beta+\delta)}{\alpha+\delta} \\ &= \alpha+(\alpha+\beta+\delta)\Big[1-\frac{\alpha}{\alpha+\delta}\Big] \ > \ 0. \end{aligned} \tag{3.78}$$

If (3.75) has a pair of real eigenvalues ρ_1, ρ_2, then $\rho_1\rho_2 > 0$ and $\rho_1 + \rho_2 < 0$, so we have $\rho_1 < 0, \rho_2 < 0$ and the DFE is a stable node and is also hyperbolic. Writing

$$c_1 \ = \ \alpha+\lambda\Big(\frac{1}{\sigma_N}-1\Big), \, c_2 \ = \ \alpha\lambda\Big(\frac{1}{\sigma_N}-1\Big)-\lambda\delta$$

where $\sigma_N = \alpha/(\alpha+\delta)R_N$, we see that the discriminant of $\triangle$ is

$$\begin{aligned} D &= {c_1}^2 - 4c_2 \\ &= \Big[\alpha+\lambda\Big(\frac{1}{\sigma_N}-1\Big)\Big]^2 - 4\Big[\alpha\lambda\Big(\frac{1}{\sigma_N}-1\Big)-\lambda\delta\Big] \\ &= \Big[\alpha-\lambda\Big(\frac{1}{\sigma_N}-1\Big)\Big]^2 + 4\lambda\delta \ > \ 0. \end{aligned} \tag{3.79}$$

2. (i) is evident from [4]

(ii) at the DPE, the Jacobian is

$$J_{DPE} \ = \ \begin{pmatrix} -\alpha R_N & -\frac{\lambda}{R_N} \\ \alpha(R_N-1)-\delta & -\frac{\lambda\delta}{\alpha R_N} \end{pmatrix}. \tag{3.80}$$

The characteristic equation is

$$\triangle(\rho) \ = \ \rho^2 + d_1\rho + d_2 \ = \ 0 \tag{3.81}$$

where

$$d_1 \ = \ \alpha R_N + \frac{\lambda\delta}{\alpha R_N}, \ d_2 \ = \ \lambda(\alpha+\delta)\Big(1-\frac{1}{R_N}\Big).$$

For $R_N > 1$, we have both $d_1 > 0$, $d_2 > 0$. If the solutions $g\triangle(\rho) = 0$, ρ_1, ρ_2 are real, then $\rho_1 + \rho_2 < 0$ and $\rho_1, \rho_2 > 0$ so both must be negative, and the equilibrium is both hyperbolic and stable. On the other hand if ρ_1, ρ_2 are complex, then $\hat{\rho} = Re(\rho_1) = Re(\rho_2)$ satisfy $2\hat{\rho} = -d_1 < 0$, and the equilibrium is again hyperbolic (moreover it is a stable focus).

3. $R_N = 1$ implies that the DFE = DPE = (1,0). For the Jacobian at the DFE, we have characteristic polynomial $\triangle(\rho) = \rho^2 + c_1\rho$, where $c_1 > 0$. Hence eigenvalues are $-c_1$ and 0.

Absence of limit cycles:

Define the simply connected region

$$\mathcal{E} = \{(S, I) : I > 0, S \geq 0, S + I \leq 1\}$$

and $B : \mathcal{E} \to \mathbb{R} : B(S, I) = 1/I$. Note that $B \in C'(\mathcal{E})$. Thus, for $(S, I) \in \mathcal{E}$:

$$\begin{aligned} \nabla.(BF)(S,I) &= \frac{\partial}{\partial S}(Bf_1(S,I)) + \frac{\partial}{\partial I}(Bf_2(S,I)) \\ &= \frac{\partial}{\partial S}\Big(\frac{1}{I}(\alpha - \alpha S - \lambda IS)\Big) + \frac{\partial}{\partial I}\Big(\frac{1}{I}(\lambda IS - (\alpha+\beta+\delta)I + \delta(1-S))\Big) \\ &= -\lambda - \alpha\frac{1}{I} + \delta(1-S)\frac{\partial}{\partial I}\frac{1}{I} \end{aligned} \tag{3.82}$$

and (3.82) can be simplified to

$$-\Big(\frac{\alpha}{I} + \lambda + \frac{\delta(1-S)}{I^2}\Big). \tag{3.83}$$

and we can see that (3.83) is negative.

By Theorem 2, §3.9 in [65] there is no closed orbit lying entirely in $\mathcal{E}$. Note, however that

$$\mathcal{T} = \mathcal{E} \cup \{(S, 0) : 0 \leq S \leq 1\} \tag{3.84}$$

so this does not preclude the existence of a limit cycle in $\mathcal{T}$. By the forward invariance of $\mathcal{T}$ under the flow, a limit cycle in $\mathcal{T}$ must contain points in both $\mathcal{E}$ and the lower boundary $B_L = \{(S, 0) : 0 \leq S \leq 1\}$ or be restricted to the lower boundary $B_L = \{(S, 0) : 0 \leq S \leq 1\}$.

However, apart from the equilibrium (1,0), there is no subset of B_L which is invariant under the flow. Therefore any limit cycle in $\mathcal{T}$ must contain both points in $\mathcal{E}$ and in B_L. In fact, the limit cycle can only contain isolated points in B_L. Therefore, there exists $\xi = (S_0, I_0)$ with $S_0 > 0$, $I_0 > 0$, $S_0 + I_0 < 1$ on the limit cycle L and $t_0 > 0$ (possibly $t_0 = \infty$) such that $\varphi(\xi, t_0) = (S, 0)$, for some $0 \leq S < 1$, where $(S, 0) \in L$. Clearly by Lemma 3.4.2, t_0 cannot be finite. Hence $t_0 = \infty$, so

$$\lim_{t\to\infty} \varphi(\xi, t) = (S, 0) \tag{3.85}$$

which implies that the additional DPE $= (S, 0)$ is an equilibrium of the system, a contradiction as $S < 1$. Therefore there is no limit cycle in $\mathcal{T}$. This yields

Proposition 3.4.6 *(3.68) has no limit cycles in* $\mathcal{T}$.

Proof: As above. ◇

For $R_N < 1$, this enables us to show that $\omega(\xi) = F$ for all $\xi \in \mathcal{T}$.

Proposition 3.4.7 *If* $R_N < 1$, *then* $\omega(\xi) = F$ *for all* $\xi \in \mathcal{T}$.

Proof:
For $R_N < 1$, the DPE is a saddle, but is not contained in $\mathcal{T}$. There is only one equilibrium in $\mathcal{T}$, the DFE, which is a stable, hyperbolic equilibrium. Therefore, no separatrix cycle can be contained in $\mathcal{T}$. By Proposition (3.4.6), there are no limit cycles in $\mathcal{T}$. Hence, by the Generalized Poincaré Bendixson Theorem (Theorem 2, §3.9 in [65]), it follows that $\omega(\xi) =$ DFE. ◇

Consider $R_N > 1$. As before, there are two equilibrium points at DFE $= (1, 0)$: the DFE is a saddle point, while DPE is a stable equilibrium. By previous calculations, we know that the system has no limit cycle in $\mathcal{T}$. It merely remains to show that there is no separatrix cycle contained in $\mathcal{T}$. If such a separatrix cycle exists, it must be part of the unstable/stable manifold of the DFE.

Suppose that we can prove that the (local) unstable manifold points into the interior of $\mathcal{T}$, while the (local) unstable manifold approaches the DFE from below the $S-$axis, as shown in Figure 3.11. As the DFE is a hyperbolic equilibrium, the stable manifold theorem tells us that the directions of the stable and unstable manifolds of the linearisation of the system at the DFE are those of the local stable and unstable manifolds of the original system at the DFE (see Theorem 4.7 in [27]). We prove, in Lemma 3.4.9 below, that the manifolds of the linearisation have the directions that were claimed for the nonlinear system above.

It is now evident that the system cannot have a separatrix cycle. Consider $x_0 \in Int(\mathcal{T}) \cap$

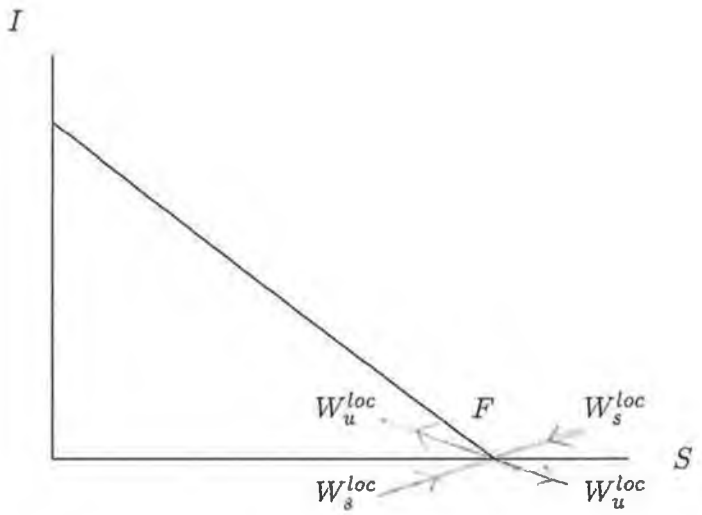

Figure 3.11: Direction of unstable manifold

$\omega_u(F)$. Then, there exists $t^* > 0$ (which can be infinite) such that $\varphi(t^*, x_0) \in \partial\mathcal{T}$ for some $(S^*, I^*) \neq F$ (note: $\varphi(t^*, x_0) = (S^*, I^*)$), a non-empty part of $\Gamma^+(x_0)$ must lie outside $\mathcal{T}$ for a cycle to exist. It now obtains that $t^* = \infty$, as $t^* < \infty$ violates Lemma 3.4.4. But as explained earlier (cf. Lemma 3.4.2) this implies that (S^*, I^*) is an equilibrium point, which is a contradiction.

Proposition 3.4.8 *If $R_N > 1$, then $\omega(\xi) = P$ for all $\xi \in \mathcal{T}/\{F\}$.*

Proof:

By the above argument, no separatrix cycle is contained in $\mathcal{T}$, and no limit cycle is in $\mathcal{T}$ by Proposition 3.4.6; therefore, by the Generalized Poincaré Bendixson Theorem, it follows for all $\xi \in \mathcal{T}$ that either

$$\omega(\xi) = P \quad or \quad \omega(\xi) = F. \tag{3.86}$$

Consider $\xi \in \mathcal{T}/\{F\}$. Then $\omega(\xi) = F$ only if ξ is on the stable manifold of the DFE. The argument preceding this proposition indicates that no part of the stable manifold of the DFE is contained in $\mathcal{T}$. Therefore we must have $\omega(\xi) = P$. ◇

Lemma 3.4.9 *Let $\mathcal{E}_u, \mathcal{E}_s$ be the unstable and stable manifolds of the linearisation of the system at the DFE. Then there exists $-1 < t_- < 0$ such that $\mathcal{E}_u = \{(x, t_- x) : x \in \mathbb{R}\}$ and*

$t_+ > 0$ *such that* $\mathcal{E}_s = \{(x, t_+x) : x \in \mathbb{R}\}$

Proof:

The stable manifold at the DFE has direction

$$x_- = \begin{pmatrix} 1 \\ -\frac{(\alpha+\rho_-)}{\lambda} \end{pmatrix}$$

where $\rho_- < 0$ and

$$x_+ = \begin{pmatrix} 1 \\ -\frac{(\alpha+\rho_+)}{\lambda} \end{pmatrix}$$

is the direction of the unstable manifold at the DFE, where $\rho_+ > 0$. To show that one branch of the unstable manifold points into the interior of $\mathcal{T}$, we must show that $0 < (\alpha+\rho)/\lambda < 1$. This is equivalent to proving $0 < \rho_+ < \lambda - \alpha$, or that $\triangle(\lambda - \alpha) > 0$, where $\triangle$ is the characteristic polynomial of the J_{DFE}, which satisfies $\triangle(\rho_\pm) = 0$.

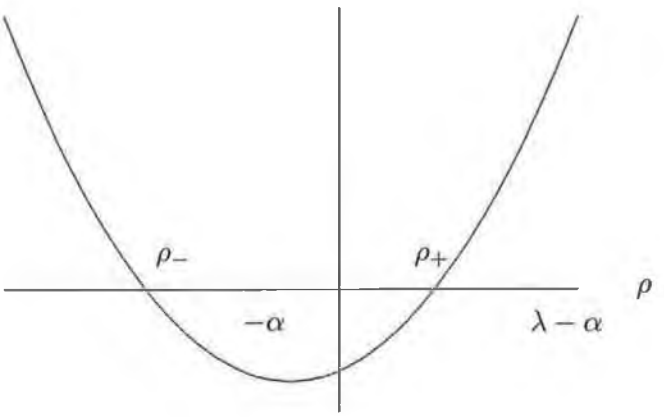

Figure 3.12: Direction of $\triangle(\rho)$

For $\rho_- < 0 < \rho_+$ we have:

- $0 > -\alpha > \rho_- \Leftrightarrow \triangle(-\alpha) < 0$
- $0 < \rho_- < \lambda - \alpha \Leftrightarrow \triangle(\lambda - \alpha) > 0$.

Since $\triangle(\rho) = \rho^2 + c_1\rho + c_2$, where c_1, c_2 are as mentioned previously, a little algebra confirms

that

$$\Delta(\lambda - \alpha) \;=\; \lambda\beta \;>\; 0, \tag{3.87}$$

as required. Note that $\lambda - \alpha > 0$, as needed, since $R_N > 1$ implies

$$\frac{\lambda}{\alpha} \;>\; \frac{\alpha + \beta + \delta}{\alpha + \delta} \;>\; 1. \tag{3.88}$$

Letting $t_- = -(\alpha + \rho_+)/\lambda$ suffices.

To show that the stable manifold cannot enter $\mathcal{T}$, it is enough to show that $(\alpha + \rho_-)/\lambda < 0$. This is equivalent to proving that $\Delta(-\alpha) < 0$. Again, it is straightforward to compute $\Delta(-\alpha) = -\lambda\delta < 0$, as needed. Putting $t_+ = -(\alpha + \rho_-)/\lambda$ suffices. ◇

Therefore, local to the DFE, the phase portrait of the linear (and hence nonlinear) system is described below.

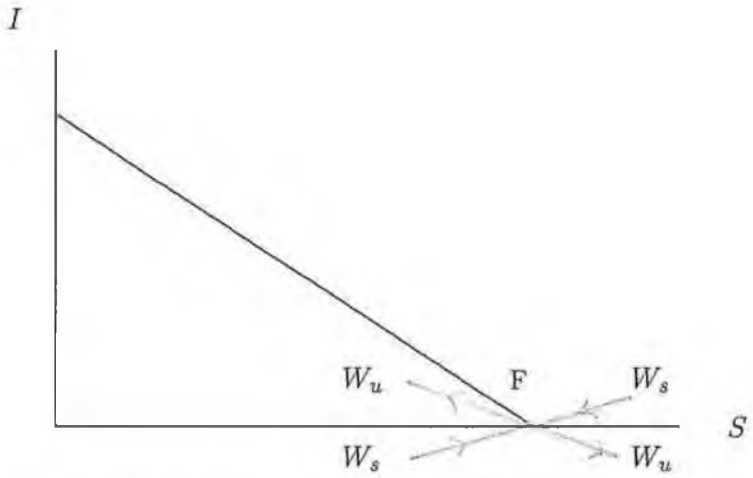

Figure 3.13: Local phase portrait to the DFE

Note:

x_+ are just the eigenvectors associated with the eigenvalues ρ_+ of the J_{DFE}.

3.4.5 An Alternative Assumption

In the models that we have looked at so far, we have set different parameters for the rate of relapse (β) and the reactivation rate (δ). Some earlier work done on AD [72], [84], [85], has

set these parameters to be equal. In modeling terms, they are assuming that *all* animals that enter the latent period will eventually become infective again, which we believe to be incorrect. If we were to take this approach, the equations in (3.47) take the form

$$S'(t) = \alpha - \lambda IS - \alpha S \tag{3.89a}$$

$$I'(t) = \lambda IS - \alpha I - \beta I + \beta L \tag{3.89b}$$

$$L'(t) = \beta I - \beta L - \alpha L \tag{3.89c}$$

From (3.89) we can calculate the reproduction ratio to be

$$R_A = \frac{\lambda(\alpha+\beta)}{\alpha(\alpha+2\beta)} \tag{3.90}$$

Comparing R_A above, with that of R_N previously calculated we can show that $R_A > R_N$. Hence, it will be more difficult to get $R_A < 1$ than R_N. As a result the disease will be more difficult to eradicate. Hence, for our model to be more accurate, we set $\beta > \delta$. Then we can show, the smaller δ is compared with β, the easier it is for R_N to remain below one.

We can also say that when we have no deaths ($\alpha = 0$), but the reactivation rate is positive ($\delta > 0$), infected individuals will either always be infectious or will visit the L compartment infinitely often. Each visit will be exponentially distributed ($e^{-\beta t}$), so the expected total time spent in L will be infinite, i.e., when $\alpha = 0$, $\delta > 0$, we have

$$R_N = \infty. \tag{3.91}$$

So, from a disease point of view, when the situation in (3.91) occurs, the disease will almost surely remain endemic in the population. In order to prevent this, when the birth and death rates are zero ($\alpha = 0$), the reactivation rate *must* be kept very small or, even better, be reduced to zero. However, if an animal survives infection from ADV, it has built up some resistance to reinfection, and is less likely to become infected, or re-infected. Hence, realistically speaking, the situation in (3.91) is unlikely to occur.

3.4.6 Reduced Graphs

In a similar way to that of the *non-vaccinated* model, we know do some graphs for the reduced model. As before, we look at graphs at various stages of an epidemic, ranging from

just beginning ($I \ll S$), to the later stages of an outbreak ($I > S$). We also look at what happens to S and I when $R_N > 1$ and $R_N < 1$ to see if the Theorems hold.

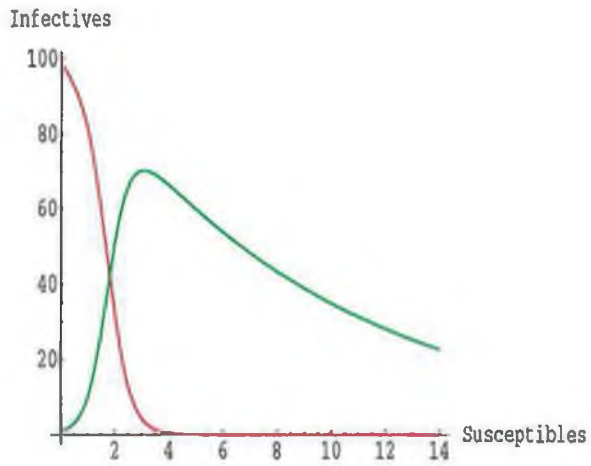

Figure 3.14: Reduced model (start of epidemic)

Here an outbreak is beginning, and we can see that immediately, the infectives increase until the threshold is reached. After this point they begin to fall away. Here $R_N = 0.3$, and we have set α to be large, if the graph continues, we have $S \to 1$ and $I \to 0$.

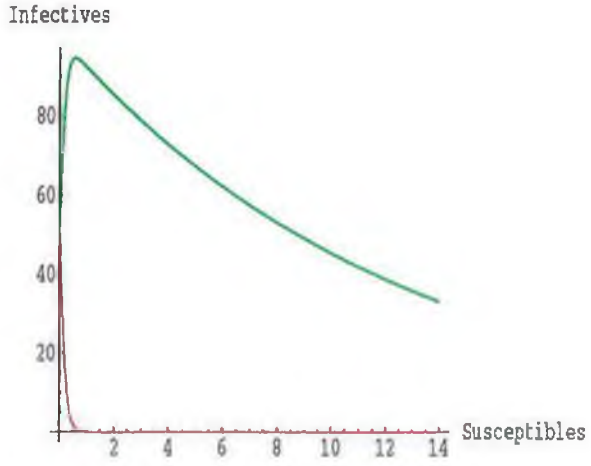

Figure 3.15: Reduced model (middle epidemic)

Here we have an even split in the population, that could go either way. At first $S = I$, but then they both die off, S more quickly, only for S to increase when $I = 0$. Here $R_N = 2$.

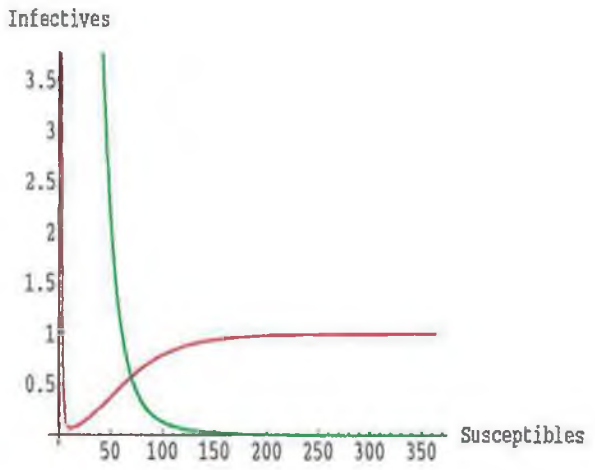

Figure 3.16: Reduced model (end epidemic)

Here we have passed saturation point in the population, in which we have more infectives than susceptibles. This graph is run for one year and as expected, $I \to 0$ (nobody to infect) and $S \to 1$ as α is increased (all newborns are susceptible).

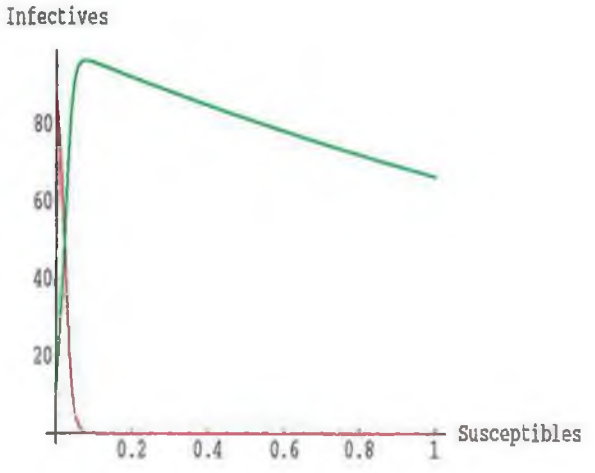

Figure 3.17: Reduced model (end epidemic)

Here we have $R_N > 2$, and as can be seen, it takes only a very short time for the susceptibles

to be reduced to zero. Eventually, $I \to 0$ for the same reasons as before, and then the susceptible population grows again.

It can be seen from Figures 3.14 to 3.17 for the reduced model, and for Figures 3.4 to 3.9 for the *non-vaccinated* model, they are only as accurate as the data that is used in them. As mentioned in Chapter 1, this was one of our main problems when we began this work, i.e. the lack of suitable data available for Irish herds. We have estimated whenever possible, but for the graphs to be as accurate as possible, the necessary data must be obtained. Until then, we can only speculate as to the accuracy of the graphs above. For instance, in the majority of the graphs above, the infected population *always* seems to die out, no matter what the initial conditions are set at. Surely, this cannot be the case *all* the time?

For the graphs in both this section and the previous one we can see that the *threshold density*, N_T, seems to be range from between 60% and 80% of the population, with the exception of Figure 3.17, where it is higher, as expected. The observations made at the start of the chapter seem to hold true also, i.e. where the spread of the disease only stops when $I = 0$. We can also see that even the slightest change in the relationship between β and δ has major implications with regards to whether the disease will remain in the population.

3.5 Vaccinated Model

3.5.1 Introduction

The purpose of a vaccine is to stimulate the immune system in such way that the response of the host to infections will be less harmful for the host [39]. The reason that we vaccinate against ADV are threefold:

- the probability of infection when exposed is greatly reduced (reduced susceptibility)
- there are fewer clinical signs when infected (clinical protection)
- there is less infectivity when infected (reduced infectivity)

The other reasons why vaccination of ADV is important are well documented at the start of Chapter 2. While vaccinated pigs can still become infected, laboratory and field experience indicate that vaccinated herds will have a significantly lower incidence of new infection [64], [86]. Indeed, studies have shown that if a vaccination programme can induce herd immunity to a degree that virus transmission in the population is sufficiently reduced, ADV will eventually be eliminated [74], [76]. In addition to the model assumptions mentioned in Section 3.2.1, we also assume that all new animals (from births and purchases) are vaccinated before being introduced into the population.

The latent period is very important when animals are vaccinated. As mentioned earlier, latentcy can be described as a period of quiescence, after which the animals may become reinfected. It has been shown that vaccination before exposure has little or not effect on the rate of establishment of virus latency, but that vaccination reduces shedding after subsequent reactivation, and it can reduce the mean duration of the infective period by up to 2 days [69], [72]. However, more recent work has proposed that using quantitative PCR assays allows the simultaneous detection and differentiation of two strains of herpesvirus. Then, a thorough understanding of the mechanisms by which vaccines prevent latency should certainly have a large impact on the efficiency of infection clean-up efforts in herds [62].

3.5.2 Vaccinated Model

From (3.27), and following the same methods that we used for the *non-vaccinated* system, we take the *vaccinated* model to be

$$\begin{aligned} S'(t) &= \alpha - (\alpha + \kappa)S && \text{(3.92a)} \\ I'(t) &= \lambda_V IP - \alpha I - \eta I + \gamma L && \text{(3.92b)} \\ L'(t) &= -\gamma L + \eta I - \alpha L && \text{(3.92c)} \\ P'(t) &= \kappa S - \alpha P - \lambda_V IP && \text{(3.92d)} \end{aligned}$$

where

$$S + I + L + P = 1. \qquad (3.93)$$

By a method similar to that used to obtain R_N in Section 3.3.1, we calculate the reproduction ratio for the *vaccinated* model from (3.92) to be

$$R_V = \frac{\lambda_V \kappa(\alpha + \gamma)}{\alpha(\alpha + \kappa)(\alpha + \eta + \gamma)}. \qquad (3.94)$$

We also calculated (3.94) using stability analysis - this is done in Appendix A. For virus eradication, it is essential that $R_V < 1$. The observation that R_V among finishing pigs vaccinated twice exceeds unity, does not, however, imply that vaccination will not succeed [76]. We now suppose that a *perfect* vaccination is available and that we are able to keep a certain fraction, q_v, vaccinated at all times. This assumption is based on anecdotal evidence from veterinarians in Ireland [44]. Then, from a disease reproduction point of view, a fraction of of contacts will be *wasted* on protected animals. We can therefore write the expected ratio for the vaccinated model as

$$E(R_V) = (1 - q_v)R_V\,. \qquad (3.95)$$

From (3.95) we can say that when

$$q_v > 1 - \frac{1}{R_V} \qquad (3.96)$$

the disease will be eradicated. In terms of R_V in (3.94) above, we write q_v as

$$q_v = \frac{[(\lambda_V \kappa - \alpha(\alpha + \kappa)](\alpha + \gamma) - \alpha\eta(\alpha + \kappa)}{\lambda_V \kappa(\alpha + \gamma)} \qquad (3.97)$$

as $\alpha \gg \gamma$, we can say $\alpha \simeq (\alpha + \gamma)$ and so (3.97) becomes

$$q_v = \frac{\lambda_V \kappa - (\alpha + \eta)(\alpha + \kappa)}{\lambda_V \kappa}. \tag{3.98}$$

3.5.3 Average level of protection

Some considerable time was spent on seeking a formula to describe the rate at which protection wears off, i.e, the rate at which animals go from the protected state to the susceptible state. Previous work on ADV modelling has not looked at this, so we were unsure of the most appropriate method to use. Finally, we assumed that the vaccine wears off exponentially. Hence we can write

$$\lambda_V(t) = \lambda(c - e^{-\nu t}) \tag{3.99}$$

where $c > 1$, t is measured in units of 1 month and ν is the *level* of vaccination, which is different from κ which is the *rate* of vaccination. In model terms, we have full vaccination when $\nu = \infty$ and no vaccination when $\nu = 0$.

We know from work previously done on optimization of vaccines [73], [85], that the best strategy is to vaccinate three times a year. Hence we can write (3.99) as an area, i.e.

$$\begin{aligned} \bar{\lambda_V} &= \frac{1}{4}\int_0^4 \lambda_V(t)dt \\ &= \frac{\lambda}{4}\Big[4c - \frac{1}{\nu}\Big(1 - e^{-4\nu}\Big)\Big] \end{aligned} \tag{3.100}$$

and we define (3.100) as the *average level of protection.* Figure 3.18 is a graphical reference to the *average level of protection.* Here we begin with a full level of vaccination, as time continues vaccination will wear off exponentially. At some point (ν_p) the farmer will revaccinate his herd (we assume that the farmer is using an optimal vaccination policy, hence he revaccinates after 4 months) and, again, we are back at full protection. Again, he will revaccinate and as before full immunity is restored.

Figure 3.15 is no longer valid if the farmer does not revaccinate on time. So, if the farmer waits for longer than the optimal time ($>$ 4 month) and the vaccination wears off, the animals would become fully susceptible. If an outbreak was to occur, the farmer would

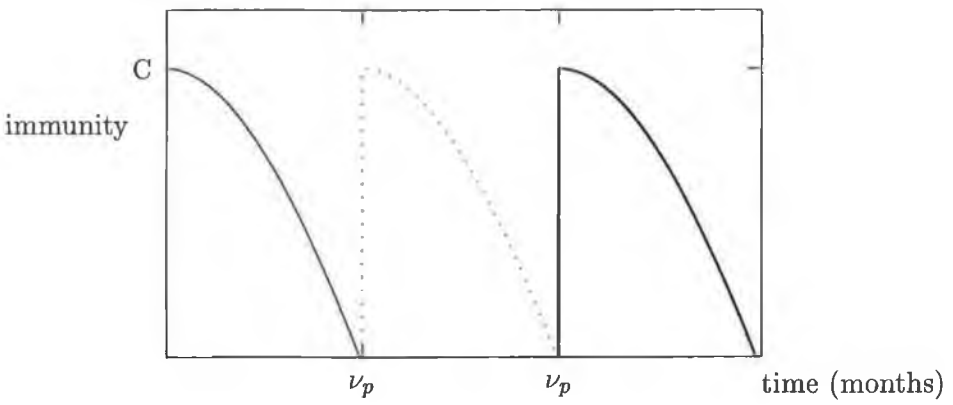

Figure 3.18: Average level of protection

have to begin the vaccination program again, as he or she would not know which animals were originally protected. Therefore it is of paramount importance that once a vaccination scheme has begun, the farmer *must* maintain it, and make sure it is optimal. Otherwise the farmer runs the risk of *actually* increasing the possibility of infection.

Consider the two extreme cases in (3.100). The first is that protection is about to wear off, which occurs as $t \to \infty$, and the second is immediately after revaccination has occurred ($t \to 0$). In the first case, we have, from (3.100), $\lambda_V(\infty) = \lambda c$. When the farmer has revaccinated, we will have $\lambda_V(0) = \lambda(c-1)$. In terms of our model, infection is $c/(c-1)$ times more likely when the protection is very low. (A range of values for λ_V can be found in Appendix C)

Note:
By manipulating the equations in (3.92) we can show, from a biological point of view, what the addition of the delay term means to the population:

- The susceptibles remain unchanged. The delay term is not in S
- The infectives will decrease because of the delay
- The latents will also decrease
- The protecteds will increase because the level of protection will rise as the delay term

slows down the outward flow.

The equations in (3.92) have two equilibrium points, the DFE

$$(S^*, I^*, L^*, P^*) = \left(\frac{\alpha}{\alpha+\kappa}, 0, 0, \frac{\kappa}{\alpha+\kappa}\right) \tag{3.101}$$

and the DPE

$$(S^*, I^*, L^*, P^*) = \left(\frac{\alpha}{\alpha+\kappa}, \frac{\alpha}{\lambda_V}(R_V - 1), \frac{\alpha\eta}{\lambda_V(\alpha+\gamma)}(R_V - 1), \frac{\kappa}{(\alpha+\kappa)R_V}\right) \tag{3.102}$$

where R_V is as before.

Theorem 3.5.1 *The DFE (3.101) always exists. (1) This equilibrium is asymptotically stable when $R_V < 1$ and unstable when $R_V > 1$. (2) When the DPE (3.102) exists, i.e. for $R_V > 1$, it is asymptotically stable.*

Biocorollary 3.5.1:
If the reproduction ratio exceeds one, all solutions (except the DFE) will approach the DPE and the disease will remain endemic in the population. Hence, the susceptible and protected fractions will decrease as the infective fraction increases, and eventually the entire population will become infected (or latent). If the reproduction ratio is less than one, all solutions approach the DFE, at which they will remain. Hence, the susceptibles and protecteds increase as the infectives decrease, and eventually the entire population will become either susceptible or protected. When the reproduction ratio equals one, only the DFE exists.

Proof:
For ease of notation we let $\lambda_V = \lambda$ and we proceed in the same manner as that of the proof of Theorem (3.4.1).

1. The linearised matrix of (3.92) is:

$$\begin{pmatrix} S \\ I \\ L \\ P \end{pmatrix}' = \begin{pmatrix} -(\alpha+\kappa) & 0 & 0 & 0 \\ 0 & \lambda P^* - (\alpha+\eta) & \gamma & \lambda I^* \\ 0 & \eta & -(\alpha+\gamma) & 0 \\ \kappa & -\lambda P^* & 0 & -(\alpha+\lambda I^*) \end{pmatrix} \begin{pmatrix} S \\ I \\ L \\ P \end{pmatrix}. \tag{3.103}$$

Putting the DFE (3.101) into (3.103) we calculate the characteristic equation to be

$$\rho^4 + f_1\rho^3 + f_2\rho^2 + f_3\rho + f_4 \;=\; 0 \tag{3.104}$$

where

$$\begin{aligned}
f_1 &= 3\alpha + \kappa + \frac{\lambda\kappa}{\alpha+\kappa}\Big(\frac{1}{R_V} - 1\Big) \\
f_2 &= \frac{(3\alpha+\kappa)\lambda\kappa}{\alpha+\kappa}\Big(\frac{1}{R_V} - 1\Big) + \alpha(3\alpha + 2\kappa) - \frac{\gamma\lambda\kappa}{\alpha+\kappa} \\
f_3 &= \alpha^2(\alpha+\kappa) + \frac{\alpha\lambda\kappa(3\alpha+2\kappa)}{\alpha+\kappa}\Big(\frac{1}{R_V} - 1\Big) - \frac{\gamma\lambda\kappa}{\alpha+\kappa}(2\alpha+\kappa) \\
f_4 &= \alpha^2\lambda\kappa\Big(\frac{1}{R_V} - 1\Big) - \alpha\gamma\lambda\kappa\,.
\end{aligned}$$

In equations f_1 to f_4 above we have slightly modified the R_V term in (3.94). We know that $\alpha \gg \gamma$, hence $\alpha \simeq (\alpha+\gamma)$. So we approximate (3.94) by

$$R_{V_1} \;=\; \frac{\lambda\kappa}{(\alpha+\kappa)(\alpha+\eta+\gamma)}\,. \tag{3.105}$$

For ease of notation, we now let $R_{V_1} = R_V$.

As before, we can use the Routh-Hurwitz test to determine the stability of (3.104) without having to solve the equation. In the notation of the Routh-Hurwitz test we have $\Delta_1 = f_1$, $\Delta_2 = f_1.f_2 - f_3$, $\Delta_3 = f_3(f_1.f_2 - f_3) - {f_1}^2.f_4$ and $\Delta_4 = f_4\,\Delta_3$.

If $\mathbf{R_V < 1}$:

If $R_V < 1$ we can show that f_1, $f_2 > 0$, hence $\Delta_1 > 0$. By rearranging f_3, we can say that for f_3 to be positive we need

$$\alpha^2(\alpha+\kappa)^2 + \lambda\kappa\Big[\alpha(3\alpha+2\kappa)\Big(\frac{1}{R_V} - 1\Big)\Big] \;>\; \gamma\lambda\kappa(2\alpha+\kappa)\,. \tag{3.106}$$

The term inside the square brackets in (3.106) is positive, as $R_V < 1$, so both sides are positive. We know that $\alpha \gg \gamma$ and so $\alpha(3\alpha+2\kappa) > \gamma(2\alpha+\kappa)$. Hence, it follows that (3.106) is true, so $f_3 > 0$.

For $\Delta_2 > 0$ we need to show that $f_1.f_2 > f_3$, i.e we need

$$\Omega_1\Omega_2 + \alpha(3\alpha+\kappa)(3\alpha+2\kappa) \;>\; \alpha^2(\alpha+\kappa) + \frac{\alpha\gamma\lambda\kappa}{\alpha+\kappa} \tag{3.107}$$

where

$$\Omega_1 \;=\; \frac{\lambda\kappa}{\alpha+\kappa}\Big(\frac{1}{R_V}-1\Big),$$

$$\Omega_2 \;=\; (3\alpha+\kappa)(\Omega_1+3\alpha+\kappa) - \frac{\gamma\lambda\kappa}{\alpha+\kappa} \tag{3.108}$$

We rearrange (3.107) as

$$\Omega_1\Omega_2 + 2\alpha(2\alpha+\kappa)^2 \;>\; \frac{\alpha\gamma\lambda\kappa}{\alpha+\kappa} \tag{3.109}$$

the right hand side of (3.109) will be small compared to the left hand side, as the $\alpha\gamma\lambda\kappa$ term will be very small. Concentrating on the left hand side of (3.109). The $2\alpha(2\alpha+\kappa)^2$ term is positive, and we know that $\Omega_1 > 0$ (as $R_V < 1$), so we are left with Ω_2. We rearrange (3.108) to give

$$(3\alpha+\kappa)(\Omega_1+3\alpha+\kappa) \;>\; \frac{\gamma\lambda\kappa}{\alpha+\kappa} \tag{3.110}$$

and we can easily show this to be true, so Ω_2 is positive. Following on from that, again omitting the $2\alpha(2\alpha+\kappa)^2$ term, and expanding the $\Omega_1\Omega_2$ term, we write (3.109) as

$$(3\alpha+\kappa)^2\Omega_1 + (3\alpha+\kappa)\Omega_1^2 \;>\; \Big(\Omega_1-\alpha\Big)\frac{\gamma\lambda\kappa}{\alpha+\kappa} \tag{3.111}$$

further expanding (3.111) we can write it as

$$\frac{\lambda\kappa\Omega_1}{\alpha+\kappa}\Big[(3\alpha+\kappa)\Big(\frac{1}{R_V}-1\Big)-\gamma\Big] + \frac{\lambda\kappa}{\alpha+\kappa}\Big[(3\alpha+\kappa)^2\Big(\frac{1}{R_V}-1\Big)-\alpha\gamma\Big] \;>\; 0 \tag{3.112}$$

as $R_V < 1$ we can show that (3.112) is true, which means that (3.111) is true, which in turn means that (3.109) is true. Hence $\Delta_2 > 0$.

We can write f_4 as

$$\alpha^2\lambda\kappa\Big[\Big(\frac{1}{R_V}-1\Big)-\frac{\gamma}{\alpha}\Big] \tag{3.113}$$

if the term inside the square bracket is positive then $f_4 > 0$. Hence, if

$$\frac{1}{R_V} \;>\; \frac{\alpha+\gamma}{\alpha} \tag{3.114}$$

then $f_4 > 0$. We write (3.114) as

$$\frac{\alpha(\alpha+\kappa)(\alpha+\gamma+\eta)}{\lambda\kappa(\alpha+\gamma)} \quad > \quad 1\,. \tag{3.115}$$

Observing (3.115) we can see that the left hand side is, in fact, $1/R_V$ before we approximated it in (3.105). As $R_V < 1$, we can say that the original R_V (in (3.94)) is also less than one. Hence (3.115) is true, which means that (3.113) is true, hence $f_4 > 0$.

In order for us to show that $\Delta_3 > 0$, we have already shown that $f_1.f_2 > f_3$, so we need to show that $f_3(f_1.f_2 - f_3) > {f_1}^2.f_4$. First, we look at ${f_1}^2.f_4$ i.e

$$(3\alpha+\kappa+\Omega_1)^2\,.\,(\alpha^2(\alpha+\kappa)\Omega_1 - \alpha\gamma\lambda\kappa) \tag{3.116}$$

where Ω_1 is as before. We have already calculated $f_1.f_2 - f_3$ to be

$$\Omega_1\Omega_2 + 2\alpha(2\alpha+\kappa)^2 \quad - \quad \frac{\alpha\gamma\lambda\kappa}{\alpha+\kappa}\,. \tag{3.117}$$

Using (3.117) and (3.116) we can write $f_3(f_1.f_2 - f_3) > {f_1}^2.f_4$, as

$$\Omega_3\Big[\Omega_1\Omega_2 + 2\alpha(2\alpha+\kappa)^2 - \frac{\alpha\gamma\lambda\kappa}{\alpha+\kappa}\Big] \quad > \quad (3\alpha+\kappa+\Omega_1)^2(\alpha^2(\alpha+\kappa)\Omega_1 - \alpha\gamma\lambda\kappa) \tag{3.118}$$

where

$$\Omega_3 \quad = \quad \alpha^2(\alpha+\kappa) + \alpha(3\alpha+2\kappa)\Omega_1 \quad - \quad \frac{\gamma\lambda\kappa}{\alpha+\kappa}\Big(2\alpha+\kappa\Big)$$

Expanding both sides of (3.118), and after some heavy computations we have

$$\pi_1{\Omega_1}^2 + \pi_2\Omega_1 + \pi_3 \quad > \quad 0 \tag{3.119}$$

where

$$\pi_1 \quad = \quad \alpha(3\alpha+2\kappa)\Omega_2 + \alpha\gamma\lambda\kappa - 2\alpha^2(\alpha+\kappa)(3\alpha+\kappa) - \alpha^2(\alpha+\kappa)\Omega_1$$

$$\begin{aligned}\pi_2 \quad = \quad & \alpha^2(\alpha+\kappa)\Omega_2 + 2\alpha^2(3\alpha+2\kappa)(2\alpha+\kappa)^2 + 2\alpha^2\gamma\lambda\kappa(3\alpha+\kappa) \\ & - \alpha^2(3\alpha+\kappa)^2(\alpha+\kappa) - \frac{\gamma\lambda\kappa}{\alpha+\kappa}\Big(\alpha^2(3\alpha+\kappa) + (2\alpha+\kappa)\Omega_2\Big)\end{aligned}$$

$$\pi_3 \quad = \quad 2\alpha^3(\alpha+\kappa)(2\alpha+\kappa)^2 + \alpha\gamma\lambda\kappa(3\alpha+2\kappa)^2 - \alpha^3\gamma\lambda\kappa - \frac{2\alpha\gamma\lambda\kappa}{\alpha+\kappa}\Big(2\alpha+\kappa\Big)^3.$$

Next we need to show if (3.119) is true or not. Starting with π_1, and using the definition of Ω_2 in (3.108) we can say

$$\begin{aligned}\pi_1 &= \alpha(3\alpha+2\kappa)(3\alpha+\kappa)+\alpha\gamma\lambda\kappa-\alpha^2(\alpha+\kappa)\Big[2(3\alpha+\kappa)+\Omega_1\Big] \\ &\quad -\frac{\alpha\gamma\lambda\kappa}{\alpha+\kappa}\Big(3\alpha+2\kappa\Big) \end{aligned} \tag{3.120}$$

and we can rewrite (3.120) as

$$\begin{aligned}\pi_1 &= \alpha(3\alpha+\kappa)\Big[\underbrace{(3\alpha+\kappa)(3\alpha+2\kappa)-2\alpha(\alpha+\kappa)}_{\theta_1}\Big]+\alpha\gamma\lambda\kappa\Big[\underbrace{1-\frac{3\alpha+2\kappa}{\alpha+\kappa}}_{\theta_2}\Big] \\ &\quad +\alpha\Omega_1\Big[\underbrace{(3\alpha+\kappa)(3\alpha+2\kappa)-(\alpha+\kappa)}_{\theta_3}\Big]. \end{aligned} \tag{3.121}$$

As all parameters in (3.121) are positive, we concentrate on $\theta_1, \theta_2, \theta_3$, to determine the sign of π_1. Expanding θ_1 gives

$$\theta_1 = \alpha(\alpha+\kappa)[7\alpha^2+7\alpha\kappa+2\kappa^2] \tag{3.122}$$

which is positive. Similarly,

$$\theta_2 = 9\alpha^2+9\alpha\kappa+2\kappa^2-(\alpha+\kappa) \tag{3.123}$$

which is also positive, and

$$\theta_3 = -\alpha\gamma\lambda\kappa(2\alpha+\kappa) \tag{3.124}$$

which is negative. However, by expanding θ_1 in (3.122), we can show that $\theta_1 > \theta_3$. Hence, adding equations (3.122) to (3.124) we can say that $\pi_1 > 0$.

Moving onto, π_2, we can write this as

$$\begin{aligned}\pi_2 &= \Omega_2\Big[\underbrace{\alpha^2(\alpha+\kappa)-\frac{\gamma\lambda\kappa}{\alpha+\kappa}\Big(2\alpha+\kappa\Big)}_{\epsilon_1}\Big]+\alpha^2\gamma\lambda\kappa\Big[\underbrace{2(3\alpha+\kappa)-\frac{3\alpha+2\kappa}{\alpha+\kappa}}_{\epsilon_2}\Big] \\ &\quad +\alpha^2\Big[\underbrace{2(3\alpha+2\kappa)(2\alpha+\kappa)^2-(3\alpha+\kappa)^2(\alpha+\kappa)}_{\epsilon_3}\Big]. \end{aligned} \tag{3.125}$$

We can write

$$\epsilon_1 = \alpha^4+\kappa(2\alpha+\kappa)(\alpha^2-\gamma\lambda) \tag{3.126}$$

which is positive. Similarly,

$$\epsilon_2 = 3(\alpha+\kappa)(\alpha+\kappa) - 3(\alpha+2\kappa) \tag{3.127}$$

which is also positive. Finally, expanding ϵ_3, we get

$$15\alpha^3 + 21\alpha^2\kappa + 11\alpha\kappa^2 + 2\kappa^3 \tag{3.128}$$

which is also positive. Hence, adding equations (3.126) - (3.128) we can say that $\pi_2 > 0$.

Finally, we have

$$\pi_3 = \alpha\gamma\lambda\kappa\Big[\underbrace{(3\alpha+\kappa)^2 - \alpha^2}_{\tau_1}\Big] + 2\alpha(2\alpha+\kappa)^2\Big[\underbrace{\alpha^2(\alpha+\kappa) - \frac{\gamma\lambda\kappa}{\alpha+\kappa}\Big(2\alpha+\kappa\Big)}_{\tau_2}\Big] \tag{3.129}$$

From inspection $\tau_1 > 0$, and we can write τ_2 as

$$\tau_2 = \alpha^4 + \kappa(\alpha^2 - \gamma\lambda)(2\alpha+\kappa) \tag{3.130}$$

which is certainly positive, hence $\pi_3 > 0$. Now that we know $\pi_1, \pi_2, \pi_3 > 0$, we can combine (3.121), (3.125) and (3.129) to say that (3.119) is true, hence we have *finally* shown $\triangle_3 > 0$. We know that $\triangle_4 = f_4.\triangle_3$, and as we have shown that both f_4 and $\triangle_3$ are positive, hence $\triangle_4 > 0$.

$$\Rightarrow \triangle_i > 0 \ \forall \ i \in [1,4]$$
$$\Rightarrow Re(\rho_i) < 0$$

Using Theorem A.1.2 we can show that ρ_i are asymptotically stable when they are < 0. Hence the DFE (3.101) is asymptotically stable when $R_V < 1$.

If $R_V > 1$:

If $R_V > 1$ we see that $f_1 > 0$ and $f_4 < 0$, hence $\triangle_1 > 0$. We know that $\triangle_4 = f_4.\triangle_3$ and $f_4 < 0$. Hence, if $\triangle_3 > 0$, then $\triangle_4 < 0$ and if $\triangle_3 < 0$ then $\triangle_4 > 0$. So, using the converse of the Routh-Hurwitz test we can say that not all principal minors are positive, hence not all eigenvalues have negative real part.

Hence, we can say that there exists at least one eigenvalue with positive real part. As one eigenvalue is positive we can use Theorem A.1.2, to say that the DFE (3.101) is unstable when $R_V > 1$.

(2) Putting the DPE (3.102) into (3.103) we calculate the characteristic equation to be

$$\rho^4 + g_1\rho^3 + g_2\rho^2 + g_3\rho + g_4 = 0 \tag{3.131}$$

where

$$\begin{aligned} g_1 &= \alpha(2 + R_V) + \kappa \\ g_2 &= \alpha\Omega_4 + \frac{\lambda\kappa}{(\alpha+\kappa)}\Big(\alpha - \frac{(\alpha+\gamma)}{R_V}\Big) \\ g_3 &= \alpha^2 R_V(\alpha+\kappa) + (2\alpha+\kappa)\frac{\lambda\kappa}{(\alpha+\kappa)}\Big(\alpha - \frac{(\alpha+\gamma)}{R_V}\Big) \\ g_4 &= \alpha^2\lambda\kappa\Big(1 - \frac{1}{R_V}\Big) - \frac{\alpha^2\gamma\lambda\kappa}{\alpha+\kappa} \end{aligned}$$

where R_V is as before and

$$\Omega_4 = (1 + R_V)(\alpha + \kappa) + R_V$$

Again using the notation of the Routh-Hurwitz test we have $\triangle_1 = g_1$, $\triangle_2 = g_1.g_2 - g_3$, $\triangle_3 = g_3(g_1.g_2 - g_3) - {g_1}^2.g_4$ and $\triangle_4 = g_4\,\triangle_3$.

If $R_V > 1$:

If $R_V > 1$ then we can see that $g_1, g_2, g_3 > 0$, hence $\triangle_1 > 0$. For $g_4 > 0$ we need

$$1 - \frac{1}{R_V} > \frac{\gamma}{\alpha+\kappa} \tag{3.132}$$

and we can write (3.132) as

$$\frac{1}{R_V} < \frac{\alpha+\kappa-\gamma}{\alpha+\kappa}. \tag{3.133}$$

Earlier in this proof, we used the approximation $\alpha \simeq \alpha + \gamma$, now, using the fact that $\alpha+\kappa \simeq \alpha+\kappa-\gamma$, we can write (3.133) as $1/R_V < 1$, which is true as $R_V > 1$, hence (3.133) and (3.132) are true, hence $g_4 > 0$.

For $\triangle_2 > 0$ we need $g_1.g_2 > g_3$, and we can write this as

$$(2\alpha + \kappa + \alpha R_V)(\Omega_4 - \Omega_1) > \alpha R_V(\alpha+\kappa) - (2\alpha+\kappa)\Omega_1 \tag{3.134}$$

where Ω_1, Ω_4 are as before. We can rearrange (3.134) as

$$\Omega_4(2\alpha+\kappa+\alpha R_V) \quad > \quad \alpha R_V(\alpha+\kappa+\Omega_1) \tag{3.135}$$

and we can further reduce (3.135) to

$$\alpha {R_V}^2(1+\alpha+\kappa)+(2\alpha+\kappa)\Omega_4 \quad > \quad \alpha R_V\Omega_1 \tag{3.136}$$

as $R_V > 1$, we can say that (3.136) is true, hence (3.134) is true, so $\triangle_2 > 0$.

For $\triangle_3 > 0$ we have already shown that $g_1.g_2 > g_3$ in (3.134), so we need to show that

$$g_3(g_1.g_2-g_3) \quad > \quad {g_1}^2.g_4\,. \tag{3.137}$$

We know that both sides of (3.137) are positive, so starting with ${g_1}^2.g_4$, and using the approximation that we calculated for g_4 in (3.133) we can write this as

$$-\alpha^2(\alpha+\kappa)\Omega_1(2\alpha+\kappa+\alpha R_V)^2 \tag{3.138}$$

and we can write (3.137) as

$$((2\alpha+\kappa)+\alpha R_V)\Omega_5 \quad > \quad \alpha R_V(\alpha+\kappa+\Omega_1) \tag{3.139}$$

where

$$\Omega_5 \quad = \quad \Omega_4+\alpha^2(\alpha+\kappa)(2\alpha+\kappa+\alpha R_V)\Omega_1\,. \tag{3.140}$$

We can write (3.140) as

$$R_V[\alpha+\kappa)(1+R_V)+1]+\alpha^2(2\alpha+\kappa+\alpha R_V)(1-R_V) \tag{3.141}$$

and we can write (3.141) as

$$(\alpha+\kappa)(1-\alpha^2)+R_V[1+\alpha+\kappa-\alpha^2]\,. \tag{3.142}$$

As all parameters $\in (0,1)$, we can show that (3.142) to be positive, hence (3.140) is also positive, hence the left hand side of (3.139) is positive. We can write the right hand side (3.139) as

$$\alpha(\alpha+\kappa)^2R_V+\alpha\lambda\kappa(1-R_V)\,. \tag{3.143}$$

We know that $R_V > 1$, hence the second term in (3.143) is negative. We can write (3.139) as

$$\alpha\lambda\kappa R_V + ((2\alpha + \kappa) + \alpha R_V)\Omega_5 \quad > \quad \alpha(\alpha + \kappa)^2 R_V + \alpha\lambda\kappa \tag{3.144}$$

as $R_V, \Omega_5 > 0$, we can rearrange (3.144) to show that it is true. Hence, $\Delta_3 > 0$. As $g_4 > 0$, we can say that $\Delta_4 > 0$.

$$\Rightarrow \Delta_i \quad > \quad 0 \quad \forall \quad i \quad \in \quad [1,4]$$
$$\Rightarrow Re(\rho_i) \quad < \quad 0$$

Using Theorem A.1.2 we can show that ρ_i are asymptotically stable when they are < 0. Hence the DPE (3.102) is asymptotically stable when $R_V < 1$. ◇

3.5.4 Vaccinated Graphs

In this section we look at some graph of the vaccinated model that we have just studied. The initial conditions will be the same as that for all the graphs that we have done previously, and now that we have an extra compartment, P, and the brown line will represent the protecteds. In all the following graphs, we assume that there is at least one infective.

In Figure 3.19 the introduction of an infective causes L to rises and not I. This would lead one to think that there is about to be an outbreak in the population, even though we are vaccinating. However, then L begins to decrease, and if the graph is run over a longer period, we see that $S, P \to 0.5$ of the population. This could be due to an overestimation of the parameter η, which measures loss of infectiousness.

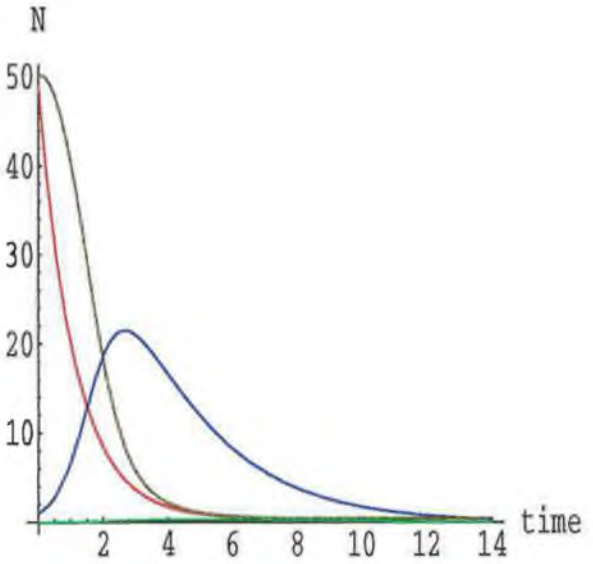

Figure 3.19: Full vaccination ($\nu = 1$)

Here we have $\nu = 1$, i.e full vaccination in the population. Hence, $\lambda_V = 0.05$, and we have a vaccination rate, $\kappa = 0.5$, as half of the population are already protected.

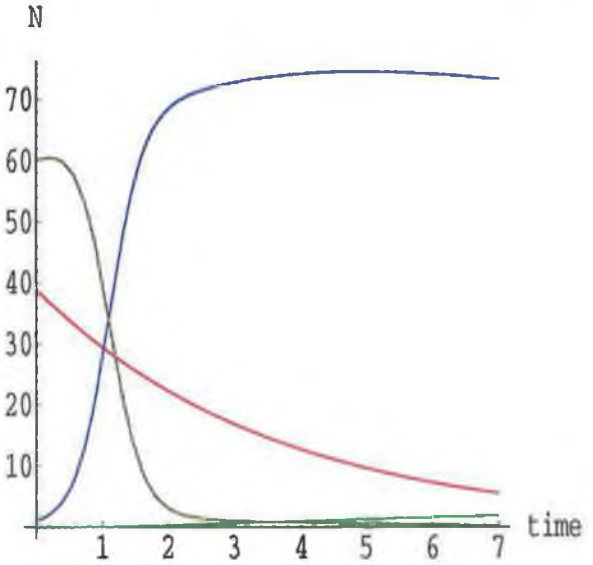

Figure 3.20: Full vaccination ($\nu = 0.75$)

In this graph we have replaced α with α_w, where $\alpha_w = (1+\alpha)^{1/52} - 1$ as we did in Figure 3.11. Here we have $\nu = 0.75$, hence $\lambda_v = 0.06$ and $\kappa = 0.25$.

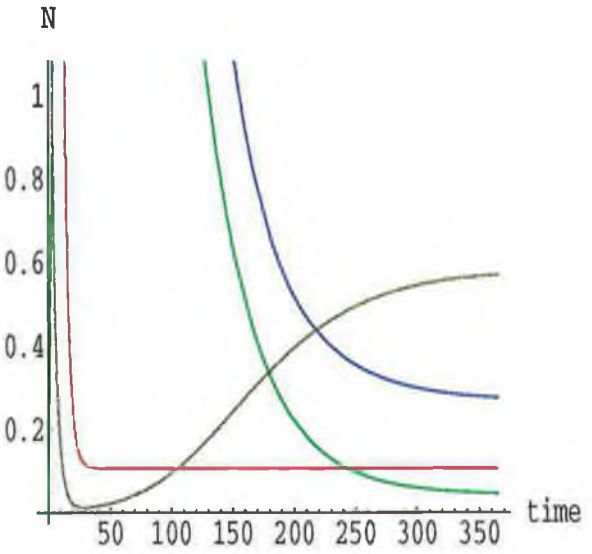

Figure 3.21: Full vaccination (longer, $\nu = 0.75$)

This graph has the same initial conditions as Figure 3.20, but we have run it for one year. Notice, how after an initial rise, the infectives and the latents decrease, albeit slowly, while the protecteds rise. Eventually, $S \to 0.15$, $I, L \to 0$ and $P \to 0.85$.

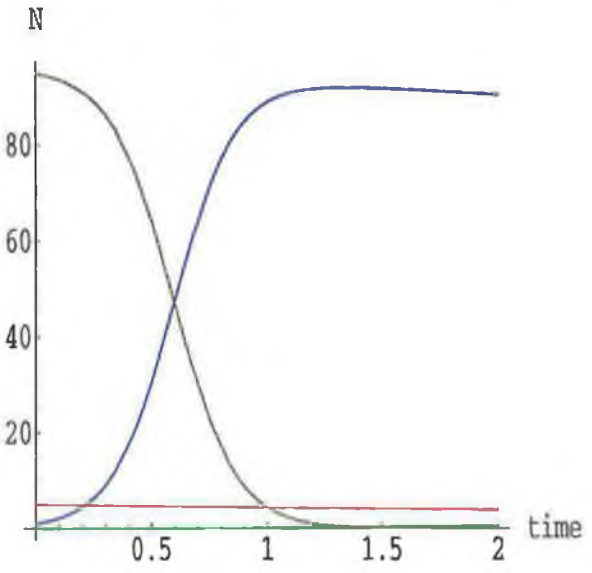

Figure 3.22: Full vaccination ($\nu = 0.25$)

Here we look at what happens as we come to the end of the vaccination period. We see the protecteds are decreasing rapidly while the latents are increasing.

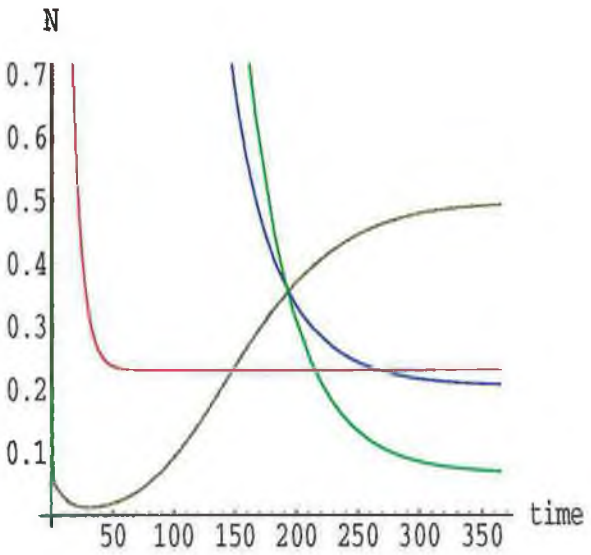

Figure 3.23: Full vaccination (longer, $\nu = 0.25$)

Running Figure 3.22 over a longer period of time, we can see that the protecteds will eventually increase, but the disease will remain in the population, as opposed to dying out, which will happen in Figure 3.21.

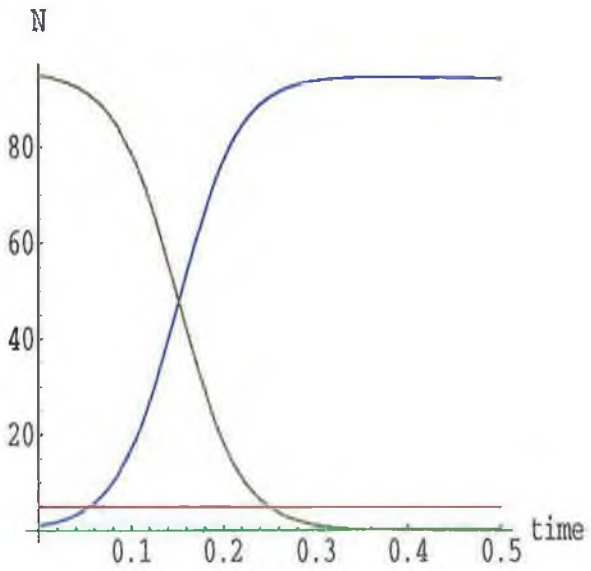

Figure 3.24: Full vaccination ($\nu = 0.01$)

Here we are at the end of the vaccination period, and there is no revaccination. In this case, $P \to 0$, $L \to 1$ *FOUR* times faster than it does in Figure 3.22. Eventually, after three years,

all animals become susceptible.

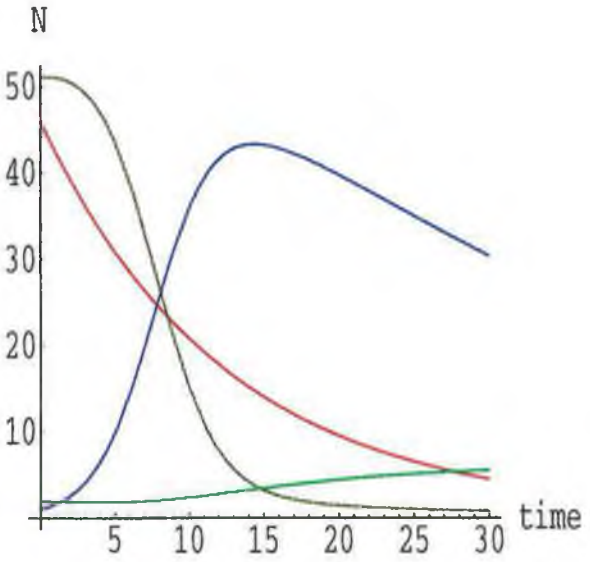

Figure 3.25: Middle Vaccination ($\nu = 0.5$)

This is an interesting graph, as both $\sigma, R_V < 1$, with $\lambda_v = 0.01$, but S, P decrease almost immediately. Eventually, S, P increase, but why they decrease at the beginning could again be due to an overestimation of some of the parameters.

3.5.5 Reduced Model

For computational ease we reduce the system in (3.92) to a 3 × 3, using (3.93) to give

$$S'(t) = \alpha - (\alpha + \kappa)S \tag{3.145a}$$

$$I'(t) = \lambda_V IP - (\alpha + \eta + \gamma)I + \gamma(1 - S - P) \tag{3.145b}$$

$$P'(t) = \kappa S - \alpha P - \lambda_V IP \tag{3.145c}$$

where, once again,

$$S + I + L + P = 1. \tag{3.146}$$

The equations in (3.145) have two equilibrium points, the DFE

$$(S^*, I^*, P^*) = \left(\frac{\alpha}{\alpha + \kappa}, 0, \frac{\kappa}{\alpha + \kappa}\right) \tag{3.147}$$

and the DPE

$$(S^*, I^*, P^*) = \left(\frac{\alpha}{\alpha + \kappa}, \frac{\alpha}{\lambda_V}(R_V - 1), \frac{\kappa}{(\alpha + \kappa)R_V}\right) \tag{3.148}$$

where R_V is as before.

Theorem 3.5.2 *The DFE (3.147) always exists. (1) This equilibrium is asymptotically stable when $R_V < 1$ and unstable when $R_V > 1$. (2) When the DPE (3.148) exists, i.e. for $R_V > 1$, it is asymptotically stable.*

Biocorollary 3.5.2:

If the reproduction ratio exceeds one, all solutions (except the DFE) will approach the DPE and the disease will remain endemic in the population. Hence, the protected fraction decrease as the infective fraction increases, and eventually the entire population will become infected. If the reproduction ratio is less than one, all solutions approach the DFE, at which they will remain. Hence, the protected fraction increases as the infective fraction decreases to zero, and eventually the entire population will become susceptible. When the reproduction ratio equals one, only the DFE exists.

Proof:

The proof of this theorem is very similar to that of Theorem 3.5.1, and as such a detailed proof is unnecessary. ◇

In Theorem 3.5.1 we did not take into account the differences that can occur in λ at the beginning and end of the protection period. Now, we look at the system in (3.145) with the intention on seeing what happens at the beginning and end of the protection period. We also make the additional assumption that once the level of protection has worn off, an outbreak of the disease *will* occur. This may not necessarily be true. It may be a case that, unfortunately for ADV, the farmer has been vaccinating optimally and the animals might have built up sufficient immunity to limit the number of new infectives, thus reducing the possibility of the disease spreading. Or it may be the case that the newly infectious animals are harvested before they have a chance to spread the disease.

End of Protection / Beginning of Outbreak

At the end of the protection period, we know, from speaking with veterinarians actively working on ADV, that when a herd are fully vaccinated, the chance of a reactivation (γ) occurring is extremely small, as the chance of relapse (η) itself is very small. Hence we can ignore the γ term from our equations in (3.145). For ease of notation we set $\xi = \lambda_V(c)$ and so (3.145) becomes

$$S'(t) = \alpha - (\alpha + \kappa)S \tag{3.149a}$$

$$I'(t) = \xi IP - (\alpha + \eta)I \tag{3.149b}$$

$$P'(t) = \kappa S - \alpha P - \xi IP\,. \tag{3.149c}$$

As before we can calculate the reproduction ratio for the equations in (3.149) to be

$$R_M = \frac{\xi\kappa}{(\alpha+\eta)(\alpha+\kappa)} \tag{3.150}$$

and we can calculate the equilibrium points of (3.149) to be

$$(S^*, I^*, P^*) = \left(\frac{\alpha}{\alpha+\kappa}, 0\,\frac{\kappa}{\alpha+\kappa}\right) \tag{3.151}$$

which is the DFE, and the DPE is

$$(S^*, I^*, P^*) = \left(\frac{\alpha}{\alpha+\kappa}, \frac{\alpha}{\xi}(R_M - 1), \frac{\kappa}{(\alpha+\kappa)R_M}\right). \tag{3.152}$$

Theorem 3.5.3 *The DFE (3.151) always exists. (1) This equilibrium is asymptotically stable when $R_M < 1$ and unstable when $R_M > 1$. (2) When the DPE (3.152) exists it is asymptotically stable.*

Biocorollary 3.5.3:
If the reproduction ratio exceeds one, all solutions (except the DFE) will approach the DPE and the disease will remain endemic in the population. Hence, the susceptible and protected fractions will decrease as the infective fraction increases, and eventually the entire population will become infected. If the reproduction ratio is less than one, all solutions approach the DFE, at which they will remain. Hence, the susceptibles and protecteds increase as the infectives decrease, and eventually the entire population will become either susceptible or protected. When the reproduction ratio equals one, only the DFE exists.

Proof:
The proof of this theorem is of a similar nature to that of the proof of Theorem (3.5.1), however it is less complicated due to the fact that we have reduced the system and have omitted the γ term from our equations.

The linearised matrix of (3.149) is:

$$\begin{pmatrix} S \\ I \\ P \end{pmatrix}' = \begin{pmatrix} -(\alpha+\kappa) & 0 & 0 \\ 0 & \xi P^* - (\alpha+\gamma) & \xi I^* \\ \kappa & -\xi P^* & -(\alpha+\xi I^*) \end{pmatrix} \begin{pmatrix} S \\ I \\ P \end{pmatrix}. \tag{3.153}$$

(1) Putting the DFE in (3.151) into (3.153) we calculate the characteristic equation to be

$$\rho^3 + h_1\rho^2 + h_2\rho + h_3 = 0 \tag{3.154}$$

where

$$h_1 = 2\alpha + \kappa + \frac{\xi\kappa}{\alpha+\kappa}\Big(\frac{1}{R_M} - 1\Big)$$

$$h_2 = \alpha(\alpha+\kappa) + (2\alpha+\kappa)\frac{\xi\kappa}{\alpha+\kappa}\Big(\frac{1}{R_M} - 1\Big)$$

$$h_3 = \alpha\xi\kappa\Big(\frac{1}{R_M} - 1\Big).$$

As before we apply the Routh-Hurwitz test to get $\Delta_1 = h_1$, $\Delta_2 = h_1.h_2 - h_3$ and $\Delta_3 = h_3.\Delta_2$.

If $\mathbf{R_M < 1}$:

If $R_M < 1$, then $h_1, h_2, h_3 > 0$, hence $\Delta_1 > 0$. For $\Delta_2 > 0$ we need to show that $h_1.h_2 > h_3$, i.e.

$$(2\alpha + \kappa + \Lambda_1).((2\alpha+\kappa)\Lambda_1 + \alpha(\alpha+\kappa)) > \alpha(\alpha+\kappa)\Lambda_1 \tag{3.155}$$

where

$$\Lambda_1 = \frac{\xi\kappa}{\alpha+\kappa}\Big(\frac{1}{R_M} - 1\Big).$$

Expanding the left hand side, we can write (3.155) as

$$(2\alpha+\kappa).[(2\alpha+\kappa)\Lambda_1 + \alpha(\alpha+\kappa) + {\Lambda_1}^2] > 0 \tag{3.156}$$

and we know that $\Lambda_1 > 0$, as $R_M < 1$, hence (3.156) holds, so we can say that $\Delta_2 > 0$. We know that $\Delta_3 = h_3.\Delta_2$, and we have already shown that both h_3 and Δ_2 are positive, so $\Delta_3 > 0$.

$$\Rightarrow \Delta_i > 0 \ \forall \ i \in [1,3]$$
$$\Rightarrow Re(\rho_i) < 0$$

Using Theorem A.1.2 we can show that ρ_i are asymptotically stable when they are < 0. Hence the DFE (3.151) is asymptotically stable when $R_M < 1$.

If $\mathbf{R_M > 1}$:

For $R_M > 1$, note that $h_3 < 0$. Whatever the sign of $\triangle_2$ is, $\triangle_3$ will be the opposite, as $\triangle_3 = h_3 \triangle_2$. Hence we know that not all principal minors are positive, so using the converse of the Routh-Hurwitz test, we can say that not all eigenvalues have negative real part.

Hence, we can say that there exists at least one eigenvalue with positive real part. As one eigenvalue has a positive real part we can use Theorem A.1.2, to say that the DFE (3.151) is unstable when $R_M > 1$.

(2) Putting the DPE (3.152) into (3.153) we calculate the characteristic equation to be

$$\rho^3 + j_1 \rho^2 + j_2 \rho + j_3 = 0 \tag{3.157}$$

where

$$\begin{aligned} j_1 &= \alpha(1 + R_M) + \kappa \\ j_2 &= \alpha R_M(\alpha + \kappa) + \frac{\alpha \xi \kappa}{\alpha + \kappa}\Big(1 - \frac{1}{R_M}\Big) \\ j_3 &= \alpha \xi \kappa \Big(1 - \frac{1}{R_M}\Big). \end{aligned}$$

As before we apply the Routh-Hurwitz test to get $\triangle_1 = j_1$, $\triangle_2 = j_1.j_2 - j_3$ and $\triangle_3 = j_3.\triangle_2$.

If $R_M > 1$:

When $R_M > 1$, j_1, j_2, $j_3 > 0$. Hence $\triangle_1 > 0$. For $\triangle_2 > 0$, we need $j_1.j_2 > j_3$, i.e.

$$(\alpha(1 + R_M) + \kappa) \,.\, (\alpha R_M(\alpha + \kappa) - \alpha \Lambda_1) > -\alpha(\alpha + \kappa)\Lambda_1 \tag{3.158}$$

where Λ_1 is as before. Expanding the left hand side of (3.158) we can write it as

$$(\alpha + \kappa)[(\alpha + \kappa) + \alpha R_M] > \alpha \Lambda_1 \,. \tag{3.159}$$

As $R_M > 1$, we know that $\Lambda_1 < 0$, so the right hand side of (3.159) is negative. We know that the left hand side is positive, so (3.159) is true, which means that $\triangle_2 > 0$. Hence $\triangle_3 > 0$ as both $\triangle_2 > 0$ and f_3 are positive.

$$\begin{aligned} &\Rightarrow \triangle_i > 0 \;\; \forall \;\; i \in [1, 3] \\ &\Rightarrow Re(\rho_i) < 0 \end{aligned}$$

Using Theorem A.1.2 we can show that ρ_i are asymptotically stable when they are < 0. Hence the DFE (3.151) is asymptotically stable when $R_M > 1$. $\diamond$

End of Outbreak / Beginning of Protection

For convenience, we assume that the farmer has revaccinated, which is what brings about the end of an outbreak. Just before vaccination, infected animals may make up a considerable proportion of the total population. We know that both the relapse (γ) and reactivation (η) rates will be quite prominent, but the contact rate will be reduced as there will be less susceptibles to infect. On the other hand, the vaccination rate will be high, $\lambda_V(\infty) = \lambda(c-1)$. Hence, we can right the equations in (3.145) as

$$S'(t) = \alpha - (\alpha + \kappa)S \tag{3.160a}$$

$$I'(t) = \lambda IP - (\alpha + \eta + \gamma)I + \gamma(1 - S - P) \tag{3.160b}$$

$$P'(t) = \kappa S - \alpha P - \lambda IP \tag{3.160c}$$

and we can see that the system in (3.160) is the same as the system in (3.145) so there is no need for us to prove Theorem 3.5.2 for the system in (3.160).

Now that we have looked at the system at the beginning and end of an outbreak, we can see that regardless of what the current state of the disease is in the population, the reproduction ratio, R_V, which is R_M in this instance, is still of critical importance.

3.5.6 Further Reduced Model

Integrating (3.145a) gives

$$\begin{aligned} S(t) &= e^{-(\alpha+\kappa)t}S_0 + e^{-(\alpha+\kappa)t}\int_0^t \alpha\, e^{-(\alpha+\kappa)s}ds \\ &= e^{-(\alpha+\kappa)t}\frac{\alpha}{\alpha+\kappa}\left(e^{-(\alpha+\kappa)t} - 1\right) + e^{-(\alpha+\kappa)t}S_0 \\ &= \frac{\alpha}{\alpha+\kappa} + \left(S_0 - \frac{\alpha}{\alpha+\kappa}\right)e^{-(\alpha+\kappa)t} \end{aligned} \tag{3.161}$$

The exponential term in (3.161) goes to zero as t goes to infinity for large t, so we are just left with the first term. Now if we put that into (3.145a) we can approximate the system of equations in (3.145), for large t, by the 2×2 system

$$I'(t) = \lambda_V IP - (\alpha + \eta + \gamma)I + \gamma\Big(\frac{\kappa}{\alpha+\kappa} - P\Big) \tag{3.162a}$$

$$P'(t) = \frac{\alpha\kappa}{\alpha+\kappa} - \alpha P - \lambda_V IP. \tag{3.162b}$$

The equations in (3.162) have two equilibrium points, the DFE

$$(I^*, P^*) = \Big(0, \frac{\kappa}{\alpha+\kappa}\Big) \tag{3.163}$$

and the DPE

$$(I^*, P^*) = \Big(\frac{\alpha}{\lambda_V}(R_V - 1), \frac{\kappa}{(\alpha+\kappa)R_V}\Big) \tag{3.164}$$

where R_V is as before.

Theorem 3.5.4 *The DFE (3.163) always exists. (1) This equilibrium is asymptotically stable when $R_V < 1$ and unstable when $R_V > 1$. (2) When the DPE (3.164) exists it is asymptotically stable when $R_V > 1$.*

Proof:
the proof of this theorem is very similar to that of Theorem 3.5.1. ◇

We could continue to work with the equations in (3.162), but as they are only valid for large t, it was decided not to pursue work on this model, as the model in (3.145) is more accurate. In the next section, we will look at what would happen to the equations in (3.145) and (3.162) if the disease was periodic.

3.5.7 Reduced Graphs

Now we do some graphs for the reduced models that we have looked at. As before, we look at graphs at various stages of an epidemic, ranging from just beginning ($I \ll S$), to the later stages of an outbreak ($I > S$). We also look at what happens to P and I when $R_V > 1$ and $R_V < 1$, to see if Theorems (3.5.1), (3.5.2) and (3.5.3) hold.

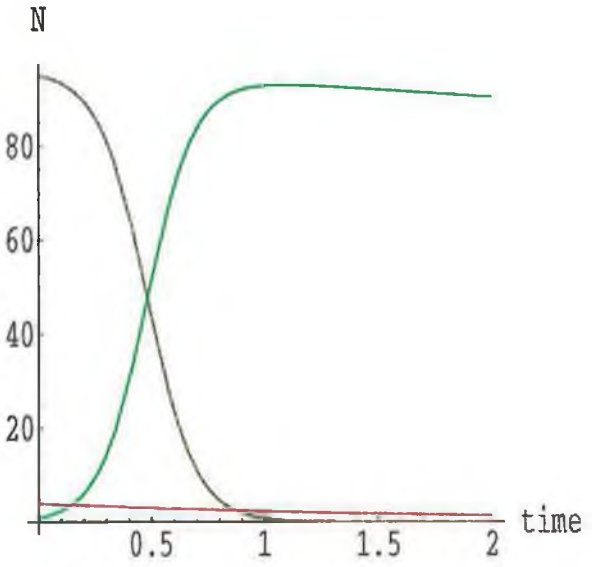

Figure 3.26: Beginning of Outbreak / End of Vaccination

In the graph above, an outbreak of the disease has just occurred and as such we have $R_V > 1$, (2.1), which means that the disease will become rampant in the population.

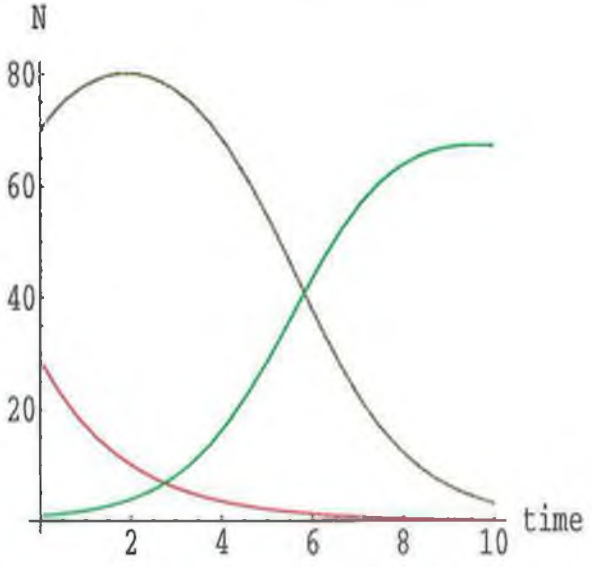

Figure 3.27: End of Outbreak / Beginning of Vaccination

Here vaccination has begun again, and the infectives are driven to zero. For some reason the infectives rise initially, with everything else falling, later (< 100 days) they begin to drop and we are just left with the protecteds, i.e. $P \to 1$.

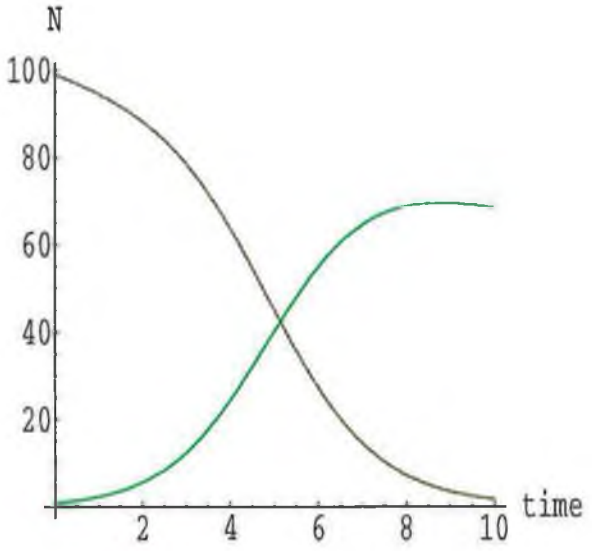

Figure 3.28: Beginning of Outbreak / End of Vaccination

In this graph, we have introduced one infective into the population, and it has had devastating consequences.

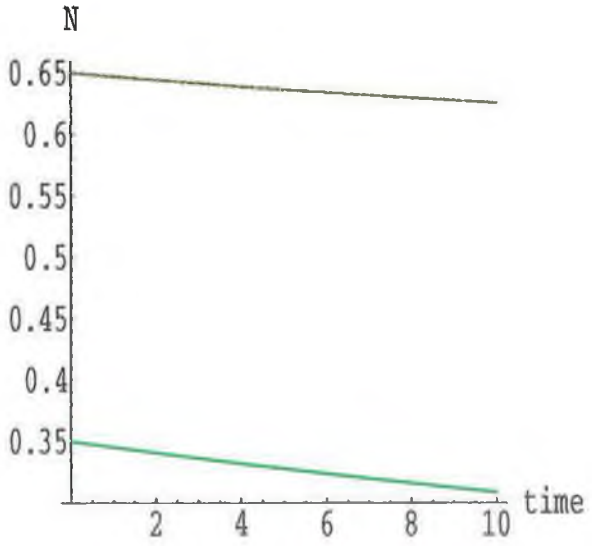

Figure 3.29: End of Outbreak / Beginning of Vaccination

Here we have re-introduced vaccination into the population, and this drives the infectives to zero. We only look at two graphs of this type as the earlier graphs are more realistic.

3.6 Periodic Infection

It has been shown that in highly concentrated herds, ADV appears to cycle continuously [79], and in some cases the reactivation of ADV from latent animals occurs periodically [52]. Some work done in [25] has shown that SEI models can have periodic solutions with incidence λIS, but not with incidence $\lambda IS/N$. To refresh the reader's memory, we began with an incidence rate of $\lambda IS/N$, but this was changed to λIS when the model was reformulated. However, as the model developed earlier is of SIL type, we are unsure as to whether or not this theory will hold. Another problem is that in Section 3.4.4 we have shown that there is no possibility of limit cycles occurring in the 2×2 *non vaccinated* model, so we have no periodic solutions in this model. We are unsure what affects this has on the *vaccinated* model.

If we consider that infection *did* occurred periodically, instead of using either (3.99) or (3.100) we introduce $\dot{a}(t)$ into the model, where $\dot{a}(t)$ is periodic in t with period T. What we are saying is that $\dot{a}(t)$ will replace λ_V in (3.145). Instead of having an infectious period when we stop vaccinating, or when the vaccination level is below a certain threshold; infection will occur periodically, regardless of vaccination. Recent work carried out in the Netherlands has shown that in sufficiently large herds, infection *will* occur regardless of whether vaccination occurs or not [77]. Here we take this a step further and assume that not only will infection occur, but that it will do so periodically. Again, much like the *average level of protection*, little work has been done on this.

If we can find a region, say $\mathcal{F}$, which contains no stationary points and which trajectories enter but do not leave, we can use the Poincaré - Bendixson Theorem to show that at least one periodic solution exists [27]. Also, according to Bendixson's criterion, if the divergence of the vector field does not change sign or does not vanish identically in some simply connected domain, say $\mathcal{F}_{\mathcal{D}}$, then periodic solutions are not possible in $\mathcal{F}_{\mathcal{D}}$ [60]. We calculate the divergence of (3.145) as

$$\frac{\partial f_1}{\partial S} + \frac{\partial f_2}{\partial I} + \frac{\partial f_3}{\partial P} = -\Big(\lambda(I-P) + (3\alpha + \eta + \gamma + \kappa)\Big). \tag{3.165}$$

Putting the DFE and DPE into (3.165) we have, starting with the DFE,

$$-\Big((3\alpha+\eta+\gamma+\kappa)-\frac{\lambda\kappa}{\alpha+\kappa}\Big) \tag{3.166}$$

which, according to Bendixson's criterion, periodic solutions are possible only when $\lambda\kappa \leq (\alpha+\kappa)(3\alpha+\eta+\gamma+\kappa)$. Putting the DPE into (3.165), we get

$$-\Big(\alpha R_V+(2\alpha+\eta+\gamma+\kappa)-\frac{\lambda\kappa}{(\alpha+\kappa)R_V}\Big), \tag{3.167}$$

which has possible periodic solutions when

$$\lambda\kappa \leq (\alpha+\kappa)R_V(\alpha(2+R_V)+\eta+\gamma+\kappa).$$

Unfortunately, as we have no realistic values of the parameters mentioned, it is difficult for us to calculate whether or not these inequalities hold.

We calculate the linearised matrix of (3.162) to be

$$\begin{pmatrix} I \\ P \end{pmatrix}' = \begin{pmatrix} \lambda P^* - (\alpha+\eta+\gamma) & \lambda I^* - \gamma \\ -\lambda P^* & -(\alpha+\lambda I^*) \end{pmatrix} \begin{pmatrix} I \\ P \end{pmatrix} \tag{3.168}$$

and we find the eigenvalues of (3.168), at the DFE, as

$$\rho = \frac{1}{2}\Big[\varphi-(\alpha+\psi)\pm\sqrt{(\alpha+\psi-\varphi)^2+4[(\alpha+\gamma)\varphi-\alpha\psi]}\ \Big] \tag{3.169}$$

where, $\psi=\alpha+\eta+\gamma$ and $\varphi=\lambda\kappa/(\alpha+\kappa)$. Letting $\varphi=\alpha+\psi$, (3.169) becomes

$$\rho = \pm\sqrt{(\alpha+\gamma)(\alpha+\psi)-\alpha\psi} \tag{3.170}$$

and we can see that the square root term in (3.169) will be positive. For bifurcation to occur, we need $b=0$ and $-4ac<0$. We can only have $b=0$ when $\varphi=\alpha+\psi$, but at this point we can see that $-4ac>0$, hence the conditions of the Hopf Bifurcation Theorem are violated, so no bifurcation exists at the DFE [80].

At the DPE, the eigenvalues of (3.168) are

$$\rho = \frac{1}{2}\Big[\varphi_1-(\alpha R_V+\psi)\pm\sqrt{(\alpha R_V+\psi-\varphi)^2+4[(\alpha+\gamma)\varphi_1-\alpha R_V\psi]}\ \Big] \tag{3.171}$$

where, ψ is as before, and $\varphi_1=\lambda\kappa/(\alpha+\kappa)R_V$. Letting $\varphi_1=\alpha R_V+\psi$, (3.171) becomes

$$\rho = \pm\sqrt{(\alpha+\gamma)(\alpha R_V+\psi)-\alpha R_V\psi} \tag{3.172}$$

and, as before, the square root term in (3.171) will be positive. So, similarly to the DFE above, we can say that no bifurcation exists at the DPE.

Introducing $\dot{a}(t)$ into the model, we can write (3.145) as

$$\begin{aligned} S'(t) &= \alpha - (\alpha+\kappa)S && \text{(3.173a)} \\ I'(t) &= \lambda\dot{a}(t)IP - (\alpha+\eta+\gamma)I + \gamma(1-S-P) && \text{(3.173b)} \\ P'(t) &= \kappa S - \alpha P - \lambda\dot{a}(t)IP. && \text{(3.173c)} \end{aligned}$$

We can say that

$$S' + I' + P' = (\alpha+\gamma)(1-(S+I+P)) - \eta I\,. \tag{3.174}$$

Next, let

$$\begin{aligned} \bar{P} &= 1-(S+I+P) \\ \Rightarrow \bar{P}' &= -(S'+I'+P') \\ \Rightarrow \bar{P}' &= -(\alpha+\gamma)\bar{P} - \eta I\,. \end{aligned} \tag{3.175}$$

For $I(0) = I_T$, $P(0) = P_T$ a T-periodic solution is admitted if $\dot{a}(t)$ is T-periodic. We can say

$$\int_0^T K'dt = K(T) - K(0) = 0 \tag{3.176}$$

for $K = I, P$.

From this we have (for I)

$$J - (\alpha+\eta+\gamma)\int_0^T I(t)dt + \frac{\gamma}{\alpha+\kappa)}T - \gamma\int_0^T P(t) = 0 \tag{3.177}$$

where

$$J = \lambda\int_0^T \dot{a}(t)I(t)P(t)dt.$$

Similarly, we can write (for P)

$$\frac{\alpha}{\alpha+\kappa}T - J - \alpha\int_0^T P(t)dt = 0. \tag{3.178}$$

Adding (3.177) and (3.178) we have

$$(\alpha+\eta+\gamma)\int_0^T I(t)dt = \Big(\frac{\alpha+\gamma}{\alpha+\kappa}\Big)T - (\alpha+\gamma)\int_0^T P(t)dt$$

$$\Rightarrow \frac{1}{T}\int_0^T I(t)dt = \frac{\alpha+\gamma}{(\alpha+\eta+\gamma)}\Big(\frac{1}{(\alpha+\kappa)} - \frac{1}{T}\int_0^T P(t)dt\Big). \tag{3.179}$$

We define the average number of infecteds as

$$\bar{I} = \frac{1}{T}\int_0^T I(t)dt$$

and the average number of protected as

$$\bar{P} = \frac{1}{T}\int_0^T P(t)dt.$$

Hence, (3.179) can be written as

$$\begin{aligned}\bar{I} &= \frac{\alpha+\gamma}{(\alpha+\eta+\gamma)(\alpha+\kappa)} - \frac{\alpha+\gamma}{\alpha+\eta+\gamma}\bar{P} \\ &= R_V\Big(\frac{1-(\alpha+\kappa)\bar{P}}{\lambda\kappa}\Big)\end{aligned} \tag{3.180}$$

where, R_V is as before, and $0 \leq \bar{I}, \bar{P} \leq 1$ and $\bar{I} + \bar{P} + \alpha/(\kappa+\alpha) \leq 1$.

3.7 Biological Implications

Throughout the course of this particularly long chapter, we have seen the critical importance of the reproduction ratio, in its various forms. This is illustrated in Theorem 3.4.5, where we can see the importance of keeping the reproduction ratio below 1. If $R_N, R_V < 1$ we have seen that the disease will die out itself, regardless of whether or not vaccination is practised. Furthermore, if a farmer is to introduce a vaccination program, it is of paramount importance that he maintains it: otherwise he runs the risk of increasing the possibility of infection.

Chapter 4

Stochastic Model

4.1 Introduction

Random perturbations may decisively affect the long-term behaviour of dynamical systems. We have already shown in Chapter 3 that we have asymptotically stable equilibrium points for both the *non-vaccinated* and *vaccinated* systems. However there may be a non-zero probability that random effects will move the system out of the domain of attraction of the equilibrium point.

In such a case, the system will eventually leave the domain of attraction with probability 1. The deterministic concept of stability no longer applies. We can replace in with the expected time elapsed before leaving the domain of attraction. This is known as the *persistence of the system* [51].

4.2 Basic Stochastic Model

Among the recent work done on stochastic modelling of infectious diseases we have studied is [7], [8], [11], [22], [26] and [53]. As far as stochastic models of ADV are concerned,we have been influenced by the work of [20], [84]. We present the main ideas of the general model here, before considering ADV in the next section. We begin with a simple population growth

model

$$\frac{d}{dt}N(t) \;=\; a(t)N(t) \tag{4.1}$$

that has initial value $N(0) = N_0$, where $N(t)$ is the size of the population and $a(t)$ is the relative growth rate. If $a(t)$ is not completely known, but subject to some random environmental effects, we write

$$a(t) \;=\; r(t) + \psi(t). \tag{4.2}$$

where $r(t)$ is the deterministic component and the random variable $\psi(t)$ is the *noise*.

Using (4.2) we write (4.1) as

$$\frac{d}{dt}N(t) \;=\; N(t)\Big[r(t) + \psi(t)\Big]. \tag{4.3}$$

Writing (4.3) in integral form we have

$$N(t) \;=\; N_0 + \int_0^t r(s)N(s)ds + \int_0^t \psi(s)N(s)ds. \tag{4.4}$$

The *noise* term in (4.4) can be expressed as $\dot{B}(t)$. We can now write (4.4) as

$$N(t) \;=\; N_0 + \int_0^t r(s)N(s)ds + \int_0^t \psi(s)N(s)dB(s) \tag{4.5}$$

and we can write (4.5) in differential form as

$$dN(t) \;=\; r(t)N(t)dt + \psi(t)N(t)dB(t) \;\text{ on t } \geq 0 \tag{4.6}$$

with initial value $N(0) = N_0$ as before.

Using Itô's formula, [26], (4.6) becomes

$$\log N(t) \;=\; \log N_0 + \int_0^t \Big(r(s) - \frac{\psi^2(s)}{2}\Big)ds + \int_0^t \psi(s)dB(s) \tag{4.7}$$

so we can calculate the implicit solution of (4.6) to be

$$N(t) \;=\; N_0 \exp\Big(\int_0^t \Big(r(s) - \frac{\psi^2(s)}{2}\Big)ds + \int_0^t \psi(s)dB(s)\Big). \tag{4.8}$$

Suppose in a population of N, there are initially $N-1$ susceptibles and 1 infective, and define $\mathcal{P}_{(S,I)}(t)$ to be the probability that there are S susceptibles and I infectives at time t. Given that the intensity of transition from state to state is independent of the past health of the animals, and that the intensity of transition depends only on the state, $\mathcal{P}_{(S,I)}(t)$ is the transition matrix of a time homogeneous Markov jump process, or continuous time Markov chain.

The initial state is fixed at $X_0 = (N, N-1)$. State at time t is $X_t \in \mathbb{R}^2_+$, then consider the state space to be

$$\mathcal{S} = \{(S,I): \ S \geq 0, I \geq 0, \ S+I \leq N\} \tag{4.9}$$

Consider $i, j \in \mathcal{S}$ and call, for $j = (S,I)$

$$\begin{aligned} \mathcal{P}_{(S,I)}(t) &:= \mathcal{P}^{ij}(t) \\ &= \mathbb{P}[X_t = j | X_0 = i] \\ &= \mathbb{P}[X_t = j] \end{aligned} \tag{4.10}$$

if A is the matrix of transition rates, then

$$\begin{aligned} \mathcal{P}'(t) &= \mathcal{P}(t)A \\ \mathcal{P}(0) &= I\,. \end{aligned}$$

Consider the state $j = (S,I)$, then

$$A_{i,(S,I)} = \begin{cases} \lambda(S+1)(I-1) & i = (S+1, I-1) \\ \beta(I+1) & i = (S, I+1) \\ -\lambda IS - \beta I & i = (S,I) \\ 0 & \text{otherwise}\,. \end{cases}$$

Thus,

$$\begin{aligned} \frac{d}{dt}\mathcal{P}_{(S,I)}(t) &= \lambda(S+1)(I-1)\mathcal{P}_{(S+1,I-1)}(t) + \beta(I+1)\mathcal{P}_{(S,I+1)}(t) \\ &\quad -(\lambda IS + \beta I)\mathcal{P}_{(S,I)}(t) \end{aligned} \tag{4.11}$$

As expected, the state (S,0) is an *absorbing state*. By this we mean a state where, once the system attains it, the system will remain there for all time. In terms of our model, we have

no infectives and I will remain at zero. Mathematically we write this as

$$\frac{d}{dt}\mathcal{P}_{(S,0)}(t) \;=\; \beta\mathcal{P}_{(S,1)}(t).$$

The expected sojourn time (temporary stay) in the state can be calculated using the following formula (from [29])

$$R_s \;=\; \inf\{t>0 : X_{t+S} \neq X_S\} \tag{4.12}$$

From (4.12) we have

$$\mathbb{P}[R_s > w | X_S = (S,I)] \;=\; e^{-\hat{\mu}(S,I)w} \tag{4.13}$$

where

$$-\hat{\mu}(S,I) \;=\; \begin{cases} \lambda IS + \beta I & \text{for } I \geq 1 \\ 0 & \text{for } I = 0. \end{cases}$$

Hence, expected sojourn time is

$$\int_{w=0}^{\infty} w \frac{d}{dw}\,\mathbb{P}[R_s \leq w | X_S = (S,I)]dw \tag{4.14}$$

and, using (4.13), we write (4.14) as

$$\int_{w=0}^{\infty} w\,\hat{\mu}(S,I)\,e^{-\hat{\mu}(S,I)w}\,dw. \tag{4.15}$$

Letting $v = \hat{\mu}(S,I)w$, (4.15) becomes

$$\int_{v=0}^{\infty} v\,e^{-v}\,\frac{1}{\hat{\mu}(S,I)}\,dv \tag{4.16}$$

which we can write as

$$\frac{1}{\hat{\mu}(S,I)}\int_0^{\infty} v\,e^{-v}dv \tag{4.17}$$

and we can see that the integral part of (4.17) is 1 when we integrate by parts. Hence, we are left with

$$\frac{1}{\hat{\mu}(S,I)} \tag{4.18}$$

Suppose there is an 'event' (i.e. transition) at time $S+w$ given that at time S, the system is in state $X_S = (S,I)$, and no transition occurred in $(S, S+w)$. Then we have, for infection,

$$\mathbb{P}[X_{S+w} = (S-1, I+1) | X_S = (S,I), R_s = w] \;=\; \frac{\lambda IS}{\lambda IS + \beta I} \tag{4.19}$$

using the fact that $R_0 = \lambda/\beta$, we can rewrite (4.19) as

$$\frac{R_0 S}{R_0 S + 1} \tag{4.20}$$

A similar method for recovery yields

$$\mathbb{P}[X_{S+w} = (S, I-1) | X_S = (S, I), R_s = w] \;=\; \frac{\beta I}{\lambda I S + \beta I} \tag{4.21}$$

again using $R_0 = \lambda/\beta$, we have

$$\frac{1}{R_0 S + 1} \tag{4.22}$$

In a method similar to that used in [22], we let $\mathcal{Q}_{(S,I)}(l)$ be the probability that the l^{th} event brought the population in state (S, I). Using (4.20) and (4.22), and provided that $I > 0$, we can say

$$\mathcal{Q}_{(S,I)}(l+1) \;=\; \begin{cases} \frac{R_0(S+1)}{R_0(S+1)+1}\,\mathcal{Q}_{(S+1,I-1)}(l) \;+\; \frac{1}{R_0 S+1}\,\mathcal{Q}_{(S,I+1)}(l), & \text{for } S > 1 \\ \frac{1}{R_0 S+1}\,\mathcal{Q}_{(S,I+1)}(l) & \text{for } S = 0, 1\,. \end{cases}$$

where

$$\mathcal{Q}_{(S,I)}(0) \;=\; \begin{cases} 1 & \text{for } S = 0, I = 1, \\ 0 & \text{otherwise.} \end{cases}$$

Following on from the calculations above, we can also introduce the R (recovered) state. Suppose that at the end of an infectious period an individual dies with probability $1 - f_i$, otherwise it enters the recovered state. Assuming that $f_i < 1$, we can do a similar calculation to that for $\mathcal{Q}_{(S,I)}(l+1)$ to find $\mathcal{Q}_{(S,I,R)}(l+1)$. Firstly, we see that

$$(S, I, R) \;=\; \begin{cases} (S-1, I+1, R) & \text{with rate} \frac{\lambda I S}{S+I+R} \\ (S, I-1, R) & \text{with rate} (1-f_i) I \\ (S, I-1, R+1) & \text{with rate} f_i I. \end{cases}$$

Now computing the probabilities with which each of the outcomes occurs, as we did for (4.20) and (4.22), we have

$$\mathcal{Q}_{(S,I,R)}(l+1) = \begin{cases} \frac{R_0(S+1)}{R_0(S+1)+S+I+R}\,\mathcal{Q}_{(S+1,I-1,R)}(l) + f_i \frac{S+I+R+1}{R_0 S+S+I+R}\,\mathcal{Q}_{(S,I+1,R-1)}(l) \\ \qquad + (1-f_i)\frac{S+I+R+1}{R_0 S+S+I+R+1}\,\mathcal{Q}_{(S,I+1,R)}(l) & \text{for } S > 1 \\ (1-f_i)\frac{S+I+R+1}{R_0 S+S+I+R+1}\,\mathcal{Q}_{(S,I+1,R)}(l) \\ \qquad + f_i \frac{S+I+R}{R_0 S+S+I+R}\,\mathcal{Q}_{(S,I+1,R-1)}(l) & \text{for } S = 0, 1\,. \end{cases}$$

From Becker [10], R_0 can be estimated at the end of an outbreak by the martingale formula

$$\frac{1}{H_t + Z_t} \sum_{i=S_t+1}^{S_0} \frac{1}{i} \tag{4.23}$$

where

S_0 = the initial number of susceptibles

S_t = the final number of susceptibles

Z_0 = the initial number of infectives (which is 0 to begin)

Z_t = the final number of infectives

H_t = the total number of infectives.

This idea may be applied to ADV as follows. From (4.23) we can calculate a formula to estimate the average number of ADV infections introduced per herd per region to be

$$\sum_{N_f}^{k=1} \frac{min(X_a, m_k)}{m_k f_k} \tag{4.24}$$

where

N_f = the number of finishing herds in the region

m = the number of compartments where specimens have been collected from herd k

f_k = the fraction of ADV introductions that results in a major outbreak for herd k.

If we look at the f_k term in (4.24) we will see that it closely resembles the *threshold density*, N_T, that was mentioned in Section 3.3.3. Hence we can say

$$\begin{aligned} f &= \frac{R_0 - 1}{R_0} \\ &= 1 - \frac{1}{R_0} \end{aligned} \tag{4.25}$$

and we can also see that (4.25) is the same as the q_v term we mentioned in Section 3.5.2.

4.3 AD Stochastic Model

Now we introduce a stochastic model corresponding with the deterministic model of AD mentioned in Chapter 3. For the stochastic model of AD we will look at the *non-vaccinated* model mentioned in Section 3.4.1. For convenience we rewrite these equations

$$S'(t) = \alpha N - \lambda \frac{IS}{N} - (\mu + E)S \tag{4.26a}$$

$$I'(t) = \lambda \frac{IS}{N} - (\mu + E)I - \beta I + \delta L \tag{4.26b}$$

$$L'(t) = \beta I - \delta L - (\mu + E)I\,. \tag{4.26c}$$

As before we introduce the scaled population sizes $x_1 = S/N$, $x_2 = I/N$, $x_3 = L/N$, and we let $\lambda_s = \lambda/N$. Using the constant population restriction ($\alpha = \mu + E$) we have $x_1 + x_2 + x_3 = 1$. Now we can reduce the equations in (4.26) to a more workable 2×2. We assume that the inflow is deterministic in the time interval $\triangle t$, and is given by $\alpha N \triangle t$, where α, N are as before. The outflow and the transmissions between the parameters will be stochastic.

We assume that in the small time interval $(t, t + \triangle t)$, S decreases by one and I increases by one because of a transition from the susceptibles to the infectives with probability $\lambda IS \triangle t$. The probability of more than one transition is $o(\triangle t)$, which can be neglected for small $\triangle t$. We can summarise the transmission in the following table:

Event	**Description**	**Probability**
$x_1 \to x_1 + 1/N$	birth of susceptible	$\alpha N \triangle t$
$x_1 \to x_1 - 1/N$, $x_2 \to x_2 + 1/N$	infection of susceptible	$\lambda_s N x_1 x_2 \triangle t$
$x_2 \to x_2 - 1/N$, $x_3 \to x_3 + 1/N$	recovery of infective	$\beta N x_2 \triangle t$
$x_3 \to x_3 - 1/N$, $x_2 \to x_2 + 1/N$	reactivation of latent	$\delta N x_2 \triangle t$
$x_1 \to x_1 - 1/N$	removal of susceptible	$\alpha N x_1 \triangle t$
$x_2 \to x_2 - 1/N$	removal of infective	$\alpha N x_2 \triangle t$
$x_3 \to x_3 - 1/N$	removal of latent	$\alpha N x_3 \triangle t$

Table 4.1: Probabilities of possible events occurring in population

From Table 4.1 we can obtain the conditional first moments of the changes of x_1 and x_2,

over the time interval Δt. We define Δx_1 to be

$$\Delta x_1 = \begin{cases} -\frac{1}{N} & \text{with probability } \lambda_s N x_1 x_2 \Delta t + \alpha x_1 N \Delta t \\ 0 & \text{with probability } 1 - \lambda_s N x_1 x_2 \Delta t - \alpha N \Delta t - \alpha x_1 N \Delta t \\ +\frac{1}{N} & \text{with probability } \alpha N \Delta t . \end{cases}$$

The standard formula for the expected value of Δx_1 is (from [26])

$$\mathbb{E}[\Delta x_1] = \sum_{j=1}^{m} \mathbb{P}[\Delta x_1 = q_j]\, q_j . \tag{4.27}$$

Hence we can calculate $\mathbb{E}[\Delta x_1]$ as

$$\begin{aligned} \mathbb{E}[\Delta x_1] &= \frac{1}{N}\alpha \Delta t.N - \frac{1}{N}\lambda_s N x_1 x_2 \Delta t - \frac{1}{N}\alpha x_1 N \Delta t + o(\Delta t) \\ &= \alpha \Delta t - \frac{1}{N}\lambda_s N x_1 x_2 \Delta t - \frac{1}{N}\alpha N \Delta t \end{aligned} \tag{4.28}$$

and, in a similar way, we can say that

$$\mathbb{E}[\Delta x_2] = \frac{1}{N}\lambda_s N x_1 x_2 \Delta t - \frac{1}{N}\beta N \Delta t + \frac{1}{N}\delta N \Delta t - \frac{1}{N}\alpha N \Delta t . \tag{4.29}$$

The reason why we do not cancel the N and $1/N$ terms in both (4.28) and (4.29) will be seen in the calculation of the second moments. For the second moments we use

$$\mathbb{E}[(\Delta x_1)^2] = \sum_{j=1}^{m} \mathbb{P}[\Delta x_1 = q_j]\, q_j^2 . \tag{4.30}$$

Using (4.30) we can say that

$$\mathbb{E}[(\Delta x_1)^2] = (\alpha \Delta t)^2 + \frac{1}{N^2}\lambda_s N x_1 x_2 \Delta t + \frac{1}{N^2}\alpha N x_1 \Delta t \tag{4.31}$$

and

$$\mathbb{E}[(\Delta x_2)^2] = \frac{1}{N^2}\lambda_s N x_1 x_2 \Delta t - \frac{1}{N^2}\beta N x_2 \Delta t + \frac{1}{N^2}\delta N x_2 \Delta t + \frac{1}{N^2}\alpha N x_2 \Delta t . \tag{4.32}$$

We can observe that the variances of Δx_1 and Δx_2 equal the second moments up to $o((\Delta t)^2)$. Now

$$\begin{aligned} b_1(t_1, x_1, x_2) &= \lim_{\Delta t \to 0} \frac{1}{\Delta t}\mathbb{E}[\Delta x_1] \\ &= \alpha - \lambda_s x_1 x_2 - \alpha x_1 \quad \text{using } \mathbb{E}[\Delta x_1] \text{ from (4.28)} \end{aligned} \tag{4.33}$$

and by the same argument

$$b_2(t_1, x_1, x_2) \;=\; \lambda_s x_1 x_2 - \beta x_2 + \delta x_2 - \alpha x_2 \,. \tag{4.34}$$

Under the assumption of continuity, we can now approximate the stochastic jump process by a system of stochastic differential equations of Itô type. By convention, such equations can be written as

$$dx_j \;=\; b_j(x_1, x_2)\, dt + \sum_{k=1}^{4} \sigma_{jk}(x_1, x_2)\, dW_t^k \,. \tag{4.35}$$

This is shorthand for the system of random integral equations

$$x_t^j \;=\; {x_0}^j + \int_0^t b_j[x_1(s), x_2(s)]\, ds \;+\; \sum_{k=1}^{4} \int_0^t \sigma_{jk}[x_1(s), x_2(s)] dW_i(s) \tag{4.36}$$

where $j = 1, 2$, $t \geq 0$, and dW_i are the increments of the independent Wiener process $W_i(t)$, $i = 1, \ldots, 4$ following [26], [53].

Our problem is to determine the functions b_j, σ_j in (4.35), (4.36). Since $(\underline{x}_t)_{t \geq 0}$ is a diffusion process, we have

$$\lim_{\triangle t \to 0} \frac{1}{\triangle t} \Big[\mathbb{E}\left[f(x_t) | X_0 = x \right] - f(x) \Big] \;=\; \mathcal{A} f(x) \tag{4.37}$$

where

$$\mathcal{A} f(x) \;=\; \frac{1}{2} \sum_{n=1}^{d} \sum_{k=1}^{d} a_{ik}(x) \frac{\partial^2 f}{\partial x_i \partial x_k} + \sum_{i=1}^{d} b_i(x) \frac{\partial f}{\partial x_i} \tag{4.38}$$

and $d = 2, (x_1, x_2)$ [53]. Using (4.37) and (4.38) with $f(x) = x$, $f(x_1, x_2) = x_1 x_2$, we have

$$\begin{aligned} \mathbb{E}\left[X_t^i - x_i \right] &= t b_i(x) + O(t) \\ \mathbb{E}\left[(X_t^i - x_i)(X_t^k - x_k) \right] &= t a_{ik}(x) + O(t) \,. \end{aligned}$$

Finally, the functions σ can be recovered from

$$a_{ik}(\underline{x}) \;:=\; \sum_{j=1}^{r} \sigma_{ij}(\underline{x}) \sigma_{kj}(\underline{x}) \tag{4.39}$$

where these are r Brownian motion; we can put $r = 4$, as from the equations in (4.26) we can see that there are four independent sources of randomness needed for both equations.

We have deaths and infectives leaving S, and we have infectives and latents entering I and deaths leaving it. One source of randomness can be used for transfer between susceptibles and infectives, but we have to use different ones for deaths as the pattern of deaths may be different in each compartment. Hence, the stochastic differential equations are of the form

$$\begin{aligned} dX_t^1 &= b_1(X_t^1, X_t^2)\,dt + \sigma_{11}(X_t^1, X_t^2)\,dW_t^{(1)} + \sigma_{12}(X_t^1, X_t^2)\,dW_t^{(2)} \qquad (4.40) \\ dX_t^{(2)} &= b_2(X_t^1, X_t^2)\,dt + \sigma_{21}(X_t^1, X_t^2)\,dW_t^{(1)} + \sigma_{23}(X_t^1, X_t^2)\,dW_t^{(3)} \\ &\quad + \sigma_{24}(X_t^1, X_t^2)\,dW_t^{(4)}\,. \qquad (4.41) \end{aligned}$$

where we assume that the randomness in the susceptible-infective transition is driven by the Brownian motion dW_1, the removal from the susceptibles by dW_2, and from the infectives by dW_4, while the random component of the transfer to latents is driven by dW_3.

Using (4.39) we have

$$\begin{aligned} a_{11}(\underline{x}) &= \sum_{j=1}^{4} \sigma_{1j}(\underline{x})\sigma_{1j}(\underline{x}) \\ &= \sigma_{11}(\underline{x})^2 + \sigma_{12}(\underline{x})^2 \qquad (4.42) \end{aligned}$$

and is a similar way to that of the calculation of (4.42) we have

$$\begin{aligned} a_{12}(\underline{x}) &= \sigma_{11}(\underline{x})^2 + \sigma_{21}(\underline{x})^2, \\ a_{21}(\underline{x}) &= \sigma_{11}(\underline{x}) \cdot \sigma_{21}(\underline{x}) = a_{12}(\underline{x}), \\ a_{22}(\underline{x}) &= \sigma_{21}(\underline{x})^2 + \sigma_{23}(\underline{x})^2 + \sigma_{24}(\underline{x})^2 \end{aligned}$$

We can calculate a_{11}, a_{22} from the second order moments

$$\begin{aligned} \mathbb{E}\left[(X_{t+h}^1 - X_t^1)^2 | \mathcal{F}_t\right] &= \mathbb{E}\left[(\triangle x_1)^2\right] \\ &= \frac{1}{N}\lambda_s x_1 x_2 h + \frac{1}{N}\alpha x_1 h + o(h^2). \qquad (4.43) \end{aligned}$$

Thus

$$\begin{aligned} a_{11}(\underline{x}) &= \lim_{h\to 0} \frac{1}{h}\,\mathbb{E}\left[(X_1(t+h) - x_1(t))^2\right] \ (X_1 = (x_1, x_2, x_3) \\ &= \frac{1}{N}\lambda_s x_1 x_2 + \frac{1}{N}\alpha x_1\,. \qquad (4.44) \end{aligned}$$

Similarly we can show that

$$a_{22}(\underline{x}) = \frac{1}{N}\lambda_s x_1 x_2 + \frac{1}{N}\beta x_2 + \frac{1}{N}\alpha x_2 . \tag{4.45}$$

We need to calculate the cross product term

$$\mathbb{E}[\triangle x_1 \triangle x_2] = \sum \mathbb{P}[\triangle x_1 = p_j, \triangle x_2 = q_j] p_j q_j . \tag{4.46}$$

We know that $\triangle x_1 = -1/N$, and $\triangle x_2 = 1/N$. Hence (4.46) can be written as

$$\begin{aligned}\mathbb{E}[\triangle x_1 \triangle x_2] &= \mathbb{P}\Big[\triangle x_1 = \frac{1}{N}, \triangle x_2 = \frac{1}{N}\Big].\frac{1}{N^2} + \mathbb{P}\Big[\triangle x_1 = \frac{1}{N}, \triangle x_2 = -\frac{1}{N}\Big].-\frac{1}{N^2} \\ &+ \mathbb{P}\Big[\triangle x_1 = -\frac{1}{N}, \triangle x_2 = \frac{1}{N}\Big].-\frac{1}{N^2} \\ &+ \mathbb{P}\Big[\triangle x_1 = -\frac{1}{N}, \triangle x_2 = -\frac{1}{N}\Big].\frac{1}{N^2}\end{aligned} \tag{4.47}$$

and we can write (4.47) as

$$\begin{aligned}\mathbb{E}[\triangle x_1 \triangle x_2] &= \alpha N \triangle t . \delta N x_2 \triangle t \frac{1}{N^2} + \alpha N \triangle t \Big(\alpha N x_2 \triangle t + \beta N x_2 \triangle t\Big).-\frac{1}{N^2} \\ &+ \lambda_s N x_1 x_2 \triangle t .-\frac{1}{N^2} + \alpha N x_1 \triangle t\,(o(\triangle t)\text{terms}) + o((\triangle t)^2)\end{aligned} \tag{4.48}$$

Because removal and both outflows are independent we must have

$$\begin{aligned}\mathbb{P}\Big[\triangle x_1 = p_j, \triangle x_2 = q_j\Big] &= \mathbb{P}\Big[\triangle x_1 = p_j\Big].\mathbb{P}\Big[\triangle x_2 = q_j\Big] \\ &= \triangle t . \triangle t \\ &= o((\triangle t)^2) .\end{aligned} \tag{4.49}$$

But we assumed at the beginning of the section that terms of $o((\triangle t)^2)$ or higher, were sufficiently small enough to be ignored. Hence some of the terms in (4.48) can be ignored, which leaves us with

$$\mathbb{E}[\triangle x_1 \triangle x_2] = -\lambda_s x_1 x_2 \triangle t \frac{1}{N} \tag{4.50}$$

Talking the limit of (4.50) as $\triangle t \to 0$, we have

$$\begin{aligned}a_{12}(\underline{x}) &= \lim_{\triangle t \to 0} \frac{1}{\triangle t}\mathbb{E}[-\lambda_s x_1 x_2 \triangle t \frac{1}{N}] \\ &= -\frac{\lambda_s}{N} x_1 x_2\end{aligned} \tag{4.51}$$

which is the desired result.

Random terms associated with outflows from S and I are independent (by hypothesis), so by considering (4.44), (4.45), we see that we must have

$$\begin{aligned}\sigma_{12}(\underline{x})^2 &= \frac{1}{N}\alpha x_1 \\ \sigma_{22}(\underline{x})^2 &= \frac{1}{N}\alpha x_2 .\end{aligned}$$

Note that we can take either plus or minus, since $-\mathcal{W}_t$ is a standard Brownian motion whenever $\mathcal{W}_t$ is a standard Brownian motion.

Returning to the transition probabilities mentioned in Table 4.1, we specifically concentrate on the removal probability ($\alpha x_2 \triangle t$). Because the process of removal is independent of outflow (and also transition between I and S), we require another *independent* source of randomness; this is why we introduce another Brownian motion $\mathcal{W}_3$, independent of $\mathcal{W}_2, \mathcal{W}_4$. This means that

$$\sigma_{23}(\underline{x})^2 = \frac{1}{N}\beta x_2$$

where, as before, the sign of $\mathcal{W}_3$ does not matter. Finally, we introduced another independent source, for the infection probability ($\lambda_s x_1 x_2 \triangle t$), $\mathcal{W}_1$. Thus

$$\begin{aligned}\sigma_{11}(\underline{x})^2 &= \frac{1}{N}\lambda_s x_1 x_2 \\ \sigma_{22}(\underline{x})^2 &= \frac{1}{N}\lambda_s x_1 x_2 . \\ \sigma_{21}(\underline{x})^2 &= \frac{1}{N}\lambda_s x_1 x_2 \qquad (4.52)\end{aligned}$$

so that

$$\sigma_{11}(\underline{x})\sigma_{21}(\underline{x}) = -\frac{1}{N}\lambda_s x_1 x_2 \qquad (4.53)$$

and thus

$$\begin{aligned}\sigma_{11}(\underline{x}) &= \nu\sqrt{\frac{1}{N}\lambda_s x_1 x_2} \\ \sigma_{21}(\underline{x}) &= -\nu\sqrt{\frac{1}{N}\lambda_s x_1 x_2}\end{aligned}$$

where $\nu = \pm 1$.

Now that we know what all the a_{ij} terms are, we are able to find the corresponding σ_{ij} terms, and combining these we can now write down the stochastic differential equations

$$dx_1 = (\alpha - \lambda_s x_1 x_2 - \alpha x_1)dt - \sqrt{\frac{1}{N}\lambda_s x_1 x_2}\, d\mathcal{W}_1 - \sqrt{\frac{1}{N}\alpha x_1}\, d\mathcal{W}_2 \tag{4.54a}$$

$$dx_2 = (\lambda_s x_1 x_2 - \alpha x_1 + \beta x_2)dt + \sqrt{\frac{1}{N}\lambda_s x_1 x_2}\, d\mathcal{W}_1 - \sqrt{\frac{1}{N}\beta x_1}\, d\mathcal{W}_3 - \sqrt{\frac{1}{N}\alpha x_2}\, d\mathcal{W}_4 \tag{4.54b}$$

where $d\mathcal{W}_i$ are the increments of the independent Wiener process $\mathcal{W}_i(t)$, $i = 1, \ldots, 4$.

The equations in (4.54) are the stochastic version of the reduced SIL model that we mentioned in Chapter 3. As can be seen from the calculations above, even the most basic stochastic model is very complicated. For instance, a number of independent sources of randomness had to be introduced to account for the various interactions that take place between compartments. For example, the birth/death rate, α, used in the deterministic model, is replaced with three different rates in the equations above, i.e. $\alpha x_1 dt$, $-\sqrt{\frac{1}{N}\alpha x_1}\, d\mathcal{W}_2$, and $-\sqrt{\frac{1}{N}\alpha x_2}\, d\mathcal{W}_4$.

Given the time restrictions it was decided to just concentrate on the deterministic model that was developed in Chapter 3. The stochastic model may be further extended to a stochastic delay differential equation model. Here X_t would have been replaced by $X_{t-\nu}$, where ν is the delay term mentioned in Section 3.5.3. This is different to the delay term that we mentioned in Chapter 3, as we have averaged our delay there whereas here we have not.

Chapter 5

Future Work / Conclusions

In this chapter we make our concluding comments about the work done in the previous chapters. We also consider possible extensions and improvements to our model. There are a number of possibilities that can be examined. With the proposed eradication program due to commence shortly, the author feels that it would be very beneficial if some of these areas were explored in more detail.

5.1 Reduce Population Restriction

Firstly, we reduce the constant population restriction that we had in Chapter 3. So instead of the birth rate (α) and the death rate ($\mu + E$) being equal, we will have two separate terms. Hence, we can write the *vaccinated* model in (3.92) as

$$\begin{aligned} S'(t) &= \alpha - (\mu + E)S - \kappa S && \text{(5.1a)} \\ I'(t) &= \lambda_V IP - (\mu + E)I - \eta I + \gamma L && \text{(5.1b)} \\ L'(t) &= -\gamma L + \eta I - (\mu + E)L && \text{(5.1c)} \\ P'(t) &= \kappa S - (\mu + E)P - \lambda_V IP. && \text{(5.1d)} \end{aligned}$$

For computational ease we set $\mu_c = \mu + E$. In a similar method to that used to compute R_N and R_V we can calculate R_C, which is the reproduction ratio for the *non-vaccinated* model

with the constant population restriction relaxed, to be

$$R_C = \frac{\lambda_V \alpha \kappa (\mu_c + \gamma)}{(\mu_c)^2 (\mu_c + \kappa)(\mu_c + \eta + \gamma)}. \tag{5.2}$$

The equations in (5.1) have two equilibrium points, the DFE

$$(S^*, I^*, L^*, P^*) = \left(\frac{\alpha}{\mu_c + \kappa}, 0, 0, \frac{\alpha\kappa}{\mu_c(\mu_c + \kappa)}\right) \tag{5.3}$$

and the DPE

$$(S^*, I^*, L^*, P^*) = \left(\frac{\alpha}{\kappa_c}, \frac{\mu_c}{\lambda_V}(R_C - 1), \frac{\mu_c \eta}{\lambda_V(\mu_c + \gamma)}(R_C - 1), \frac{\alpha\kappa}{\mu_c \kappa_c R_C}\right) \tag{5.4}$$

where, $\kappa_c = \mu_c + \kappa$.

Theorem 5.1.1 *The DFE (5.3) always exists. (1) This equilibrium is asymptotically stable when $R_C < 1$ and unstable when $R_C > 1$. (2) When the DPE (5.4) exists it is asymptotically stable when $R_C > 1$ and unstable when $R_C < 1$.*

Proof:
The proof of this theorem is very similar to that of Theorem 3.4.1. The main difference is that the α terms are replaced by $\mu + E$. The computations are more intense, but the desired result can be obtained. ◇

However, farmers like to maximise their output, so animals are usually fully housed, i.e if one animal died during the finishing stage, it would be replaced by another animal. As mentioned in Chapter 2, pigs are farmed on an all in - all out basis, so our constant population assumption that $\alpha = \mu + E$ is not unrealistic. The author feels that it would be not be in the best interests to pursue this area further, as time could be spent working on one of the following areas that we are about to discuss.

5.2 Environmental Capacity

In the model in Chapter 3, we decided to neglect the environmental capacity of ADV. There are a number of reasons why this was done. Firstly, the majority of the modelling work

done on ADV has also adopted this approach. However, some work on modelling with the environmental capacity has been done by [71], [72], but their stability analysis results are open to question.

Secondly, and most importantly, the main reason that this was not included in our model is the fact that the majority of Irish farms are intensive pig producing units. This means that no other animals are housed on the farms, and as such the transmission capacity of ADV to other animals is very much reduced. Another reason was that there are no wild boar in Ireland, and it has been shown that wild boar reduce the effectiveness of eradication [70], [87].

From an ADV point of view, such a model is important in a German context, where wild boar are a major problem [87], and also in Illinois, where raccoons are carriers of AD [92], along with other wildlife [90]. Other diseases, such as tuberculosis in badgers [61] have encountered similar eradication difficulties. If we had incorporated the environmental capacity into our model, the *vaccinated* system in (3.92) would have become

$$\begin{aligned} S'(t) &= \alpha - \alpha S - \kappa S && \text{(5.5a)} \\ I'(t) &= \lambda_V IP - (\alpha + \eta + \eta_c)I + \gamma L + \alpha_c E_c && \text{(5.5b)} \\ L'(t) &= -\gamma L + \eta I - \alpha L && \text{(5.5c)} \\ P'(t) &= \kappa S - \alpha P - \lambda_V IP && \text{(5.5d)} \\ {E_c}'(t) &= \eta_c I - \alpha_c E_c\,. && \text{(5.5e)} \end{aligned}$$

where we have the new parameters,
η_c = rate at which the local environment is contaminated
α_c = instantaneous rate at which the virus is inactivated

Note:
$1/\eta_c$ is the mean expected time virus particles persist in the local environment. After this period elapses the virus becomes inactive and presents no danger.

We have the new term

$$E_c \quad = \quad \text{the number of infectives in the population that are shedding the virus and are contaminating the local environment.}$$

5.3 Incomplete Immunity

In Section (3.4.5) we assumed that re-infected animals transmit the disease at reduced rates to that of first time infected animals. Looking at this assumption for a different perspective, we could create a new model that would have four new compartments; first time (S_1) and subsequent time (S_2) susceptibles, and first time (I_1) and subsequent time (I_2) infectives. Instead of having the models that we have developed in Chapter 3, we would have the following

$$
\begin{aligned}
S_1{}'(t) &= \alpha(1-\phi) - S_1(\lambda_1 I_1 + \lambda_2 I_2) - \alpha S_1 && \text{(5.6a)}\\
I_1{}'(t) &= S_1(\lambda_1 I_1 + \lambda_2 I_2) - (\alpha + \delta_1) I_1 && \text{(5.6b)}\\
S_2{}'(t) &= \alpha\phi - \gamma_1 S_2(\lambda_1 I_1 + \lambda_2 I_2) + \delta_1 S_1 + \delta_2 I_2 - \alpha S_2 && \text{(5.6c)}\\
I_2{}'(t) &= \gamma_1 S_2(\lambda_1 I_1 + \lambda_2 I_2) - (\alpha + \delta_2) I_2 && \text{(5.6d)}
\end{aligned}
$$

where

$$S_1 + I_1 + S_2 + I_2 = 1$$

and we define the new parameters,

λ_1, λ_2 = the contact rate between first time and subsequent time individuals respectively

α = the birth/death rate

δ_1, δ_2 = the rate of relapse for first time and subsequent time individuals respectively

ϕ = the fraction of vaccinated individuals

γ_1 = the reducing factor on subsequent infections.

Note that the ϕ term in (5.6) is related to the q_v term that we mentioned in Section (3.5.2). Systems like (5.6) are very detailed and can be complicated to work with. It is only recently that systems of this type have been looked at with regards to eradication of various diseases [24], [28]. As was done in Chapter 3, we could have calculated the reproduction ratio for (5.6) and looked at the stability analysis of the system. We may calculate R_0 for this system using the next generation matrix, where R_0 is the dominant eigenvalue [22]. Indeed we can define R_0 to be

$$
\begin{aligned}
R_0 &= (1-\phi)\, R_1 + \phi\, R_2 \\
&= (1-\phi)\, \frac{\lambda_1}{\alpha + \delta_1} + \phi\, \frac{\gamma \lambda_2}{\alpha + \delta_2} && \text{(5.7)}
\end{aligned}
$$

Where R_1 is the basic reproduction ratio for an SIS epidemic model with no vaccination and R_2 is the basic reproduction ratio for an SIS epidemic model that contains vaccination. If time had permitted, we would have looked at this system in much more detail as it seems to be the most useful and worthwhile of the three extensions that were considered. However, some corrections would have to be made before work could begin on a model of this type, as it does not take into account the latent period, and it is unlikely that animals will continue to become reinfected throughout their entire lifetime.

Mathematics aside, the way that animals are housed could also be looked at, as we have seen in Chapter 3 that the contact rate, λ, is quite important. If animals could be housed in such a way that the comparments were better separated, the chances of meeting an infective would be lower, so ADV could be eradicated from the population much more quickly, as the infection would not have such a large base of susceptibles to infect. Other additional measures that could reduce R_0 would include: the prevention of mixing of litters, an all-in all-out policy, and a central corridor between compartments.

Another modification that might have been considered would have been to take *metapopulations* (population consists of a separate local population, by spatial or other characteristics) into account. Here we could have divided a farm up into separate compartments, e.g, breeding, fattening etc. and considered each one as a separate *metapopulation*. We could also have looked at *age-dependent models*, e.g, older pigs more resistant to the disease, unvaccinated piglets more susceptible etc. A lot of modelling work of this type has been done on AIDS [57]. The only drawback to this kind of modelling work is that a considerable amount of information is needed, and as already mentioned in our case, this information is not readily available.

The area of disease modelling has become quite exciting in recent times. It was assumed that improvements in antibiotics and vaccination programmes would soon lead to the elimination of infectious diseases. However, infectious disease agents are adapting and evolving so that newer stronger infectious agents are emerging, which results in newer diseases emerging and the resurgence of some existing diseases. Indeed the discovery of new stronger infectious agents, known as *prions*, which are thought to be the main agent of BSE and CJD, has led to a renewal of interest in mathematical modelling [33].

5.4 Conclusions

We began this thesis with the intention of creating various mathematical models for ADV in Ireland. The main objectives of our work were to look at something that has never been done in Ireland before, and to provide the reader with a more comprehensive picture of ADV worldwide. We also wanted to know what parameters were most important with regard to eradication of ADV. We showed that for all the models that were developed, R_0 (in its various form, i.e R_N, R_V etc.) was the most important term. When $R_0 > 1$, ADV will remain in the population, and will be very difficult to eradicate.

When $R_0 < 1$, the disease is much easier to work with, and from the resulting theorems in Chapter 3, we learn that the disease can be eradicated when this happens. Similarly, the sign of σ is very important, particularly in large herds, where the contact rate λ would be large. Unfortunately, we do not have enough accurate data to see what happens to the models over various time periods. As a result we can only speculate as to what the outcome will be. If there is to be any further mathematical work done on AD, this data *must* be obtained, both on a national, regional (and breeding / producing unit) scale.

We had hoped that the eradication programme would be implemented during the course of this work and we could have worked with the Department of Agriculture and the IFA in achieving this goal. If anything has been learned throughout this thesis, it is that AD *can* be eliminated from Irish herds, and can be done much more efficiently and economically than other European countries have, as we can learn from there mistakes. We hope that this work will inspire others to take an active interest in this area, and maybe someday, our initial goal of eradicating ADV in Ireland will be achieved.

The recent outbreak of various diseases in the UK (Classical Swine Fever, Foot and Mouth Disease (FMD)), previously thought to have been eradicated, farmers must now be even more vigilant if they are to survive in what is becoming an increasingly difficult industry. However, with the recent confirmation of FMD in Louth, the chances of the government giving due attention to ADV are very slim. Indeed, the author feels that it will be necessary for an ADV outbreak to occur before some official action will be taken against it.

Appendix A

Theorems and Stability Analysis

A.1 Theorems / Definitions

The author wishes that this thesis be self contained, and as a result the following definitions and theorems regarding stability are included.

Let $\mathbf{x} = \xi(t)$ be a solution of the differential equation

$$\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x}) \tag{A.1}$$

Definition A.1.1 *The solution $\mathbf{x} = \xi(t)$ of (A.1) is stable if every solution $\omega(t)$ of (A.1) which starts sufficiently close to $\xi(t)$ at $t = 0$ must remain close to $\xi(t)$ for all future time t. The solution $\xi(t)$ is unstable if there exists at least one solution $\omega(t)$ of (A.1) which starts near $\xi(t)$ at $t = 0$ but which does not remain close to $\xi(t)$ for all future time. More precisely, the solution $\xi(t)$ is stable if for every $\epsilon > 0$ there exists $\delta_s = \delta_s(\epsilon)$ such that each component*

$$|\omega_j(t) - \xi_j(t)| < \epsilon \text{ if } |\omega_j(t) - \xi_j(t)| < \delta_s(\epsilon), \quad j = 1, \ldots, n$$

for every solution $\omega(t)$ of (A.1).

The stability question can be resolved for each solution of the linear differential equation

$$\dot{\mathbf{x}} = \mathbf{A}\mathbf{x}. \tag{A.2}$$

From this we have the following theorem.

Theorem A.1.2 *(1) Every solution* $\mathbf{x} = \xi(t)$ *of (A.2) is stable if all the eigenvalues of* $\boldsymbol{A}$ *have negative real part.*
(2) Every solution $\mathbf{x} = \xi(t)$ *of (A.2) is unstable if at least one eigenvalue of* $\boldsymbol{A}$ *has positive real part.*
(3) Suppose all eigenvalues of $\boldsymbol{A}$ *have real part* ≤ 0 *and* $\rho_1 = \iota\sigma_1, \ldots, \rho_l = \iota\sigma_l$ *have zero real part. Let* $\rho_j = \iota\sigma_j$ *have multiplicity* k_j*. This means that the characteristic polynomial of* $\boldsymbol{A}$ *can be factored into the form*

$$h(\rho) \quad = \quad (\rho - \iota\sigma_1)^{k_1} \ldots (\rho - \iota\sigma_l)^{k_l} g(\rho)$$

where all the roots of $g(\rho)$ *have negative real part. Then, every solution* $\mathbf{x} = \xi(t)$ *of (A.1) is stable if* $\boldsymbol{A}$ *has* k_j *linearly independent eigenvectors for each eigenvalue* $\rho_j = \iota\sigma_j$*. Otherwise, every solution* $\xi(t)$ *is unstable.*

Proof: See [14] or [27]. ◇

In order for us to be able to use Theorem (A.1.2), we have to use the Hartman-Grobman theorem. This shows that near a hyperbolic equilibrium point $\mathbf{x_0}$, the nonlinear system

$$\dot{\mathbf{x}} \quad = \quad \mathbf{f_1}(\mathbf{x}) \tag{A.3}$$

has the same qualitative structure as the linear system in (A.2).

Theorem A.1.3 *Let* E *be an open subset of* $\mathbf{R}^n$ *containing the origin, let* $\mathbf{f_1} \in C^1(E)$ *and let* ξ_t *be the flow of the nonlinear system (A.3). Suppose that* $\mathbf{f(0)} = \mathbf{0}$ *and that the matrix* $\mathbf{A}$ *has no eigenvalue with zero real part. Then there exists a homeomorphism* $\mathcal{H}$ *of an open set* U *containing the origin onto an open set* V *containing the origin such that for each* $\mathbf{x_0} \in U$*, there is an open interval* $I_0 \subset \mathbf{R}$ *containing zero such that for all* $x_0 \subset \mathbf{R}$ *and* $t \subset I_0$

$$\mathcal{H} \circ \xi_t \quad = \quad e^{\mathbf{A}t}\mathcal{H}(\mathbf{x_0});$$

i.e., $\mathcal{H}$ *maps trajectories of (A.3) near the origin onto trajectories of (A.2) near the origin and preserves the parameterization.*

Proof: See [65]. ◇

Definition A.1.4 *A solution* $\mathbf{x} = \xi(t)$ *of (A.1) is asymptotically stable if it is stable, and if every solution* $\omega(t)$ *which starts sufficiently close to* $\xi(t)$ *must approach* $\xi(t)$ *as* t *approaches infinity. In particular, an equilibrium solution* $\mathbf{x(t)} = \mathbf{x^0}$ *of (A.1) is asymptotically stable if every solution* $\mathbf{x} = \omega(t)$ *of (A.1) which starts sufficiently close to* $\mathbf{x^0}$ *for all future time, but ultimately approaches* $\mathbf{x^0}$ *as* t *approaches infinity.*

A.2 Non Vaccinated model

Here we calculate the reproduction ratio for the *non-vaccinated* model, i.e R_N, using stability analysis as done in [72]

$$\alpha - \lambda I^* S^* - \alpha S^* = 0 \tag{A.4a}$$

$$\lambda I^* S^* - (\alpha + \beta) I^* + \delta L^* = 0 \tag{A.4b}$$

$$\beta I^* - \delta L^* - \alpha L^* = 0 \tag{A.4c}$$

From (A.4c) we get

$$L^* = \frac{\beta I^*}{(\alpha + \delta)} \tag{A.5}$$

next we put (A.5) into (A.4b) to give

$$\lambda I^* S^* - (\alpha + \beta) I^* + \frac{\beta \delta I^*}{(\alpha + \delta)} = 0. \tag{A.6}$$

Simplifying (A.6) we get

$$S^* = \frac{\alpha(\alpha + \beta + \delta)}{(\alpha + \delta)\lambda} \tag{A.7}$$

and putting (A.7) into (A.4a) we write

$$\alpha - I^* \frac{\alpha(\alpha + \beta + \delta)}{(\alpha + \delta)} - \frac{\alpha^2(\alpha + \beta + \delta)}{(\alpha + \delta)\lambda} = 0. \tag{A.8}$$

Simplifying (A.8) we get

$$I^* = \frac{\alpha}{\lambda}\Big(R_N - 1\Big), \tag{A.9}$$

where

$$R_N = \frac{\lambda(\alpha+\delta)}{\alpha(\alpha+\beta+\delta)}.$$

If the virus is to persist in the *non-vaccinated* population, i.e $I^* > 0$, which occurs when $R_N > 1$. It follows that disease eradication should occur when $R_N < 1$.

A.3 Vaccinated model

Following on from the *non-vaccinated* model, we can calculate R_V for the *vaccinated* model in a similar way

$$\alpha - (\alpha+\kappa)S^* = 0 \quad \text{(A.10a)}$$

$$\lambda_V I^* P^* - (\alpha+\eta)I^* + \gamma L^* = 0 \quad \text{(A.10b)}$$

$$-\gamma L^* + \eta I^* - \alpha L^* = 0 \quad \text{(A.10c)}$$

$$\kappa S^* - \alpha P^* - \lambda_V I^* P^* = 0. \quad \text{(A.10d)}$$

From (A.10a) we get

$$S^* = \frac{\alpha}{(\alpha+\kappa)} \quad \text{(A.11)}$$

and from (A.10c) we have

$$L^* = \frac{\eta I^*}{(\alpha+\gamma)}. \quad \text{(A.12)}$$

Put (A.12) into (A.10b) to give

$$\lambda_V I^* P^* - (\alpha+\eta)I^* + \gamma\frac{\eta I^*}{(\alpha+\gamma)} = 0. \quad \text{(A.13)}$$

Simplifying (A.13) we get

$$P^* = \frac{\alpha(\alpha+\eta+\gamma)}{\lambda_V(\alpha+\gamma)} \quad \text{(A.14)}$$

now, putting (A.11) and (A.14) into (A.10d) we get

$$\frac{\alpha\kappa}{\alpha+\kappa} - \frac{\alpha^2(\alpha+\eta+\gamma)}{\lambda_V(\alpha+\gamma)} - \frac{\alpha(\alpha+\eta+\gamma)}{(\alpha+\gamma)}I^* = 0. \quad \text{(A.15)}$$

Simplifying (A.15) we get

$$I^* = \frac{\alpha}{\lambda_V}\Big(R_V - 1\Big) \tag{A.16}$$

where

$$R_V = \frac{\lambda_V \kappa(\alpha+\delta)}{\alpha(\alpha+\kappa)(\alpha+\beta+\delta)}$$

If the virus is to persist in the *vaccinated* population, i.e $I^* > 0$, which occurs when $R_V > 1$. It follows that disease eradication will eventually occur when $R_V < 1$. We also calculated R_C and R_M in a similar way, so it is unnecessary to include it hear. In terms of the models that we have developed in Chapter 3, when $R_0 = 1$ (i.e R_N, R_V, R_M, R_C) only the DFE exists.

Appendix B

Eradication Procedures

With the possibility of a nationwide eradication program being implemented in the near future, work has begun on deciding how the scheme will be organised (Section 2.5.2). In order for us to obtain the necessary data for our model, it was decided that a questionnaire would be drawn up, with the intention of collecting the data and establishing the prevalence of AD in the National Herd, in a nationwide survey. The idea behind this questionnaire was based on a survey carried out in the United States in 1995 [9]. The questionnaire was developed with the help of a number of people actively working in the Irish pig industry (Michael Martin and Brendan Lnych of Teagasc).

The plan was to distribute one to each pig producer in Ireland. As the number of producers has declined in recent year, this would not be as big a problem as originally expected (At the time of writing there are 550 highly specialised commercial units in the country). A pre-eradication survey, carried out at farm level in 1999, showed that 96% of respondents supported a Nationwide Eradication Programme while 96.7% were willing to participate in this programme [89]. From this information it is clear that the industry is fully behind an eradication programme, and we expected the questionnaire responses to be high.

The scale of this survey was large enough to warrant an acquisition of extra funding, which was to be provided by the Irish Farmer's Association. With the EU announcement of an official deadline for an AD eradication programme to be in place, the full co-operation of the Department of Agriculture was also assured. However, subsequently the Irish Farmers

Association were unwilling to commit to this work and, after initial preparations had begun, the survey had to be abandoned.

As mentioned in Section 2.5.2, meat juice could be used in the ELISA test. A draft eradication program was designed with the object of initially eliminating circulating virus from the National Herd [42]. The intention was to do this at a minimum cost, and subsequently achieving OADF status in accordance with EU regulations. An outline of the proposed eradication programme for breeding herds is shown in Figure B1, and one for the finishing herds in Figure B2. Unfortunately, much like our survey, this draft proposal was overlooked by the Department of Agriculture.

More recent advances in the area of xenotransplantation (using animal organs as substitutes for failing human organs) have made the eradication of diseases like ADV even more important. Because of the similar size of organs, and the widespread availability, the pig is one of the most commonly used animals in xenotransplantation [6]. Putting aside the ethical issues related to this area, it is clear that if scientists can establish that animal organs can be used as a long term solution, then the need for disease free animals will be great. The Irish pig industry is of superior health status compared to the rest of mainland Europe (see Table 2.1, Section 2.3.2). If ADV was to be eradicated, we would be ideally suited to breed animals to aid in the further develop of this important work.

Towards the end of this work we learned that the EU has set a deadline of October 1st, 2001 for a Nationwide Eradication programme to be in place. Rather than acting on this, the Department of Agriculture immediately worked on obtaining an extension to this date, which was granted due to the Foot and Mouth crisis. The date has now been set as June 1st, 2002. With the threat of future trade restrictions now very real it is finally time to take ADV seriously, otherwise the consequences for the Irish Pig Industry could be devastating.

AUJESZKY'S DISEASE SURVEY

Section 1: Company Details:

1(a) Name: _____ Herd No.: _____
(Herd Owner)

1(b) Address: _____

_____

1(c) Address of Pig Farm *(if different from above)*: _____

2. Cattle herd number *(if applicable)*: _____

3. Name and telephone number of veterinary inspector / veterinary consultant

_____

_____

4. To which market do the majority of your pigs go *(please tick as appropriate)*?

Domestic ☐ European ☐ other _____ ☐

5. What type of pig farming do you specify in *(please tick one)*?

_____ ☐

6. How many pigs do you have in your unit?

(please be as specific as possible)

Number	Sows	Weaners	Breeders	Fatteners
Less than 5,000				
5,000 – 10,000				
10,000 – 15000				
15,000 – 20,000				
20,000 – 30,000				
More than 30,000				

7. At any one time, how many pigs, in total, are kept on the unit? _____

8. From where do you purchase the majority of your animals?

_____

8(a). How close is your premises to the place where you purchase animals *(please tick one)*?

< one mile ☐ 1 to 3 miles ☐ 3 to 5 miles ☐ more than five miles ☐

8(b). How close is the nearest slaughtering plant to your premises *(please tick one)*?

< one mile ☐ 1 to 3 miles ☐ 3 to 5 miles ☐ more than five miles ☐

Section 2 Biosecurity Details:

9. Do you have a perimeter fence that excludes wildlife? YES NO

10. Do domestic animals (dogs, cats etc.) have access to the production unit? YES NO

11. What disinfectant procedures do you undertake?

Disinfectant mat at entrance	YES NO
Disinfecting of truck before loading	YES NO
No unauthorized personnel entering farm	YES NO
Other _____	YES NO

12. Are visitors required to wear clothing supplied by the farm? YES NO

13. How are dead animals disposed of?

Burial	YES NO
Incineration	YES NO
Collected by dead animal collection service:	
on the farm	YES NO
at the perimeter of the farm	YES NO
Other _____	YES NO

14. How close is the nearest production unit to you *(please tick one)*?

< one mile ☐ 1 to 3 miles ☐ 3 to 5 miles ☐ more than five miles ☐

15. Where does your feed come from?

_____

16. Which of the following diseases have been present in your herd *(please tick as appropriate)*

Disease	YES / NO	Last Outbreak
Actinobacillus (Hemophilus)		
Enzootic Pneumonia		
Transmissible Gastroenteritis (TGE)		
Progressive Atrophic Rhinitis		
PRRS		
Salmonella		
Streptococcal Meningitis		
Swine Dysentery		
Swine Influenza		
Swine Vesicular Disease		

17. Who carries out the majority of vaccinations on your premises?

_____

18. Which of the following do you vaccinate against *(please tick as appropriate)*

Disease	Sows	Weaners	Breeders	Fatteners
Actinobacillus (Hemophilus)				
Enzootic Pneumonia				
PRCV / TGE				
Progressive Atrophic Rhinitis				
PRRS				
Salmonella				
Streptococcal Meningitis				
Swine Dysentery				
Swine Influenza				
Swine Vesicular Disease				

Section 3 Aujeszky's Disease Details:

19. Have you ever had any clinical outbreaks of Aujeszky's Disease? YES NO
(if YES, please tick which herds; if NO please go to question 22)

piglets ☐ sows ☐ weaners ☐ fatteners ☐

20. When did this outbreak occur *(month / year)*? _____

21. What percentage of your herd is infected with Aujeszky's Disease *(please tick one)*?

<10% ☐ between 10% and 20% ☐ more than 20% ☐

22. Do you vaccinate against Aujeszky's Disease? *(if NO, go to question 29)* YES NO

23. If yes, what type of vaccine do you use? _____

24. What type of pigs do you vaccinate *(please tick as appropriate)*?

piglets ☐ sows ☐ weaners ☐ fatteners ☐

25. Are you happy with the vaccination procedures you have? YES NO

26. If NO, what other procedures would you implement? _____

27. When purchasing new animals, which of the following would you do?

Vaccinate and quarantine for 30 days, then revaccinate YES NO
Vaccinate and introduce immediately YES NO
Introduce immediately YES NO

28. Do you purchase animals only from producers who vaccinate? YES NO

29. Do the benefits of vaccination outweigh the costs? YES NO

30. If you answered NO to either questions 19 or 22, do you have any future plans to vaccinate against Aujeszky's Disease? YES NO

31. Would you support government regulation in this area? YES NO

32. What kind of regulations would you like to see in operation?

Stricter control of pig movement	YES	NO
Herds' status levels used	YES	NO
More accurate records to be kept	YES	NO
Vaccinations made compulsory	YES	NO
Vaccination costs borne by government	YES	NO

33. With the possibility of export restrictions being placed on Irish herds in the near future, would you be happy to see a nationwide eradication program implemented? YES NO

34. In relation to Table 3 on page 7, what herd status would you consider most appropriate for your farm?

_____

35. Please feel free to make any further comments:

_____

_____

Signed _____ Date _____

Please return to:
Glenn Fingleton
School of Mathematical Sciences
Dublin City University
Dublin 9

Herd Status (1)	Test Procedure (2)	Vaccination (3)	Maintenance (4)	Movement Control (5)
Officially Aujeszky's Disease Free (OADF)	Full herd test with negative results	No vaccination for minimum of 2 years	15% monitor of the breeding animals (or 25 animals, whichever is greater) tested over the course of each year. Such testing shall be split into at least three approximately equal divisions each separated by at least two months	Purchase from OADF herds only with post movement test in isolation
Pending officially Aujeszky's Disease Free (POADF)	Full herd test with negative results	No vaccination less that 2 years	15% monitor of the breeding animals (or 25 animals, whichever is greater) tested over the course of each year. Such testing shall be split into at least three approximately equal divisions each separated by at least two months	Purchase from OADF herds only with post movement test in isolation
Aujeszky's Disease Free (ADF)	Full herd test with negative results	Vaccination practiced	15% monitor of the breeding animals (or 25 animals, whichever is greater) tested over the course of each year. Such testing shall be split into at least three approximately equal divisions each separated by at least two months	Purchase from OADF or ADF herds with post movement test in isolation
Pending Aujeszky's Disease Free (PADF)	Infected herds culling positive animals	Vaccination practiced	Testing all sows post farrowing and culling positives	Purchase from OADF or ADF herds with post movement test in isolation
Infected Breeding Herd		Vaccination compulsory	Monitoring at point of slaughter	Purchase from OADF or ADF herds with post movement test in isolation
Infected Breeding Herd		Vaccination compulsory	Monitoring at point of slaughter	Unrestricted
Monitored Herd	% of herd tested with negative results awaiting full herd test	Optional	Awaiting full herd test	Purchase from OADF or ADF herds
Non Status	Untested	Optional	Awaiting test	Unrestricted

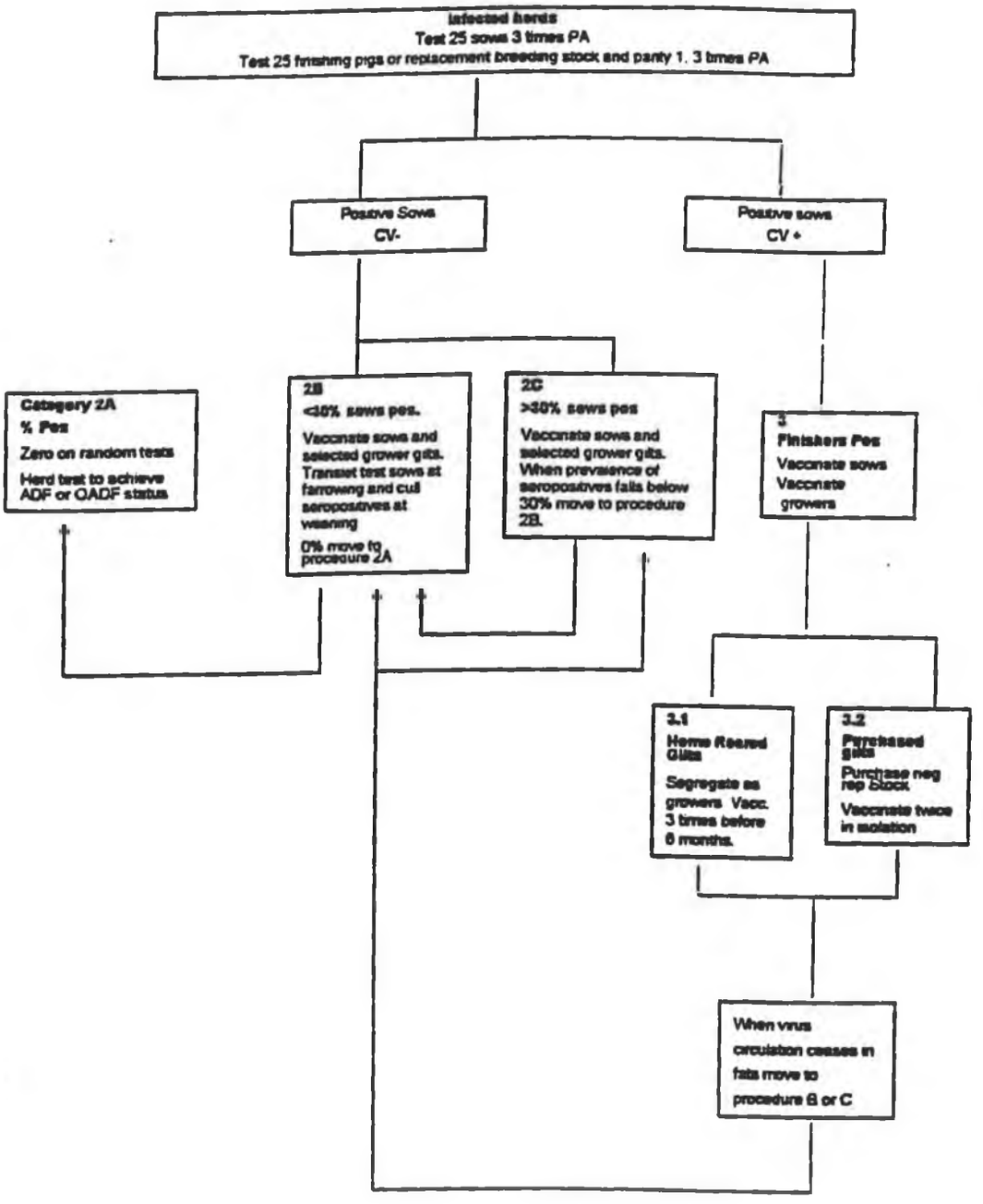

Figure B.1: Proposed Eradication program for Breeding Herds

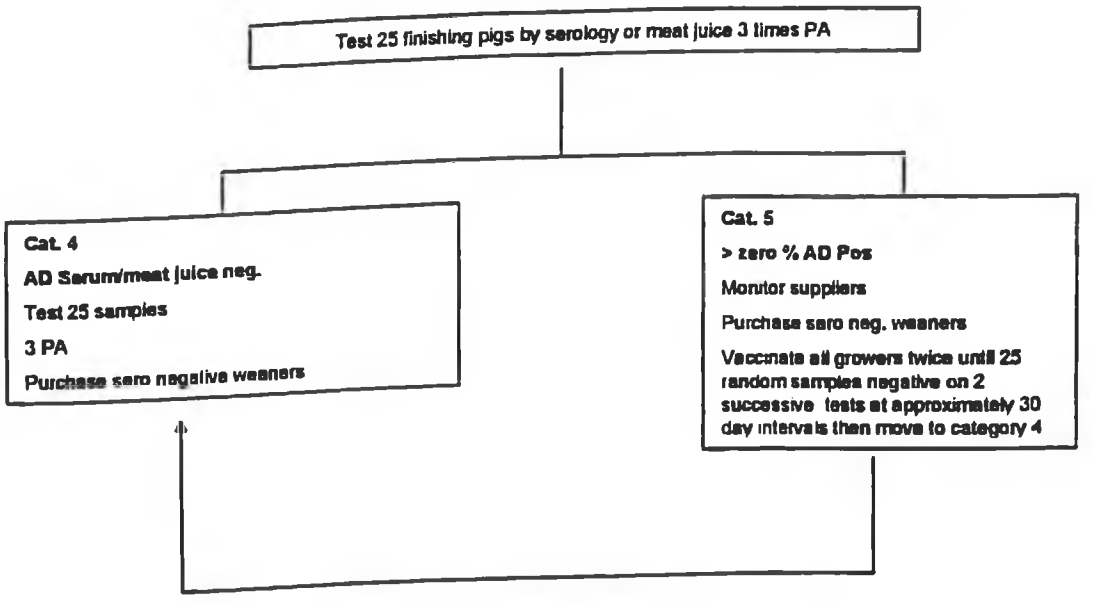

Figure B.2: Proposed Eradication program for Finishing Herds

The cost of testing, vaccination, veterinary visits and advice are influenced by the ability of the farm to eliminate ADV. This ability is greatly influenced by the Biosecurity of the farm. The cost of vaccination in a 500 sow unit increases from £4000 in a CV- herd, to £11,000 in a CV+ herd [42]. It was estimated that the total cost of a nationwide eradication program was £16,950,000, while the total cost of the proposed system is £820,000, which as the reader can see, is in stark contrast to that of the full vaccinated costs.

Appendix C

Programs

A number of different programs were used for all of the various systems that we have considered in this thesis. As they are of a similar nature, it was decided that just the two main programs would be reproduced here. In all of the programs it was necessary to use Y instead of I as I is predefined as a complex number in Mathematica.

C.1 Stability Analysis

(* This is 3×3 system when we do not vaccinate *)
(* The first thing we do is to calculate the equilibrium points of the system *)

Clear[A, $A_1, A_2, \lambda, \alpha, \delta, \beta, S, Y, L$]
eqonerhs = $-\lambda * Y[t] * S[t] + \alpha - \alpha * S[t]$;
eqtworhs = $\lambda * Y[t] * S[t] - \alpha * Y[t] - \beta * Y[t] + \delta * L[t]$;
eqthrrhs = $\beta * Y[t] - \delta * L[t] - \alpha * L[t]$;
eqpts = Solve[eqonerhs == 0, eqtworhs == 0, eqthrrhs == 0, $S[t], Y[t], L[t]$]
Simplify[eqpts]

(* next we find the linearised matrix of the above system and find its determinant *)

linmatrix = D[eqonerhs, $S[t]$], D[eqonerhs, $Y[t]$], D[eqonerhs, $L[t]$],

D[eqtworhs, $S[t]$], D[eqtworhs, $Y[t]$], D[eqtworhs, $L[t]$],
D[eqthrrhs, $S[t]$], D[eqthrrhs, $Y[t]$], D[eqthrrhs, $L[t]$] ;

MatrixForm [linmatrix]
eye = 1,0,0, 0,1,0, 0,0,1
(* where eye is the identity matrix *)
MatrixForm[linmatrix - ρ*eye]
A = Det[linmatrix - ρ*eye]

(* Then we replace the S and Y terms with the equilibrium points we have calculated above, starting with the DFE. *)

ReplaceAll[A, $S[t] \to 1, I[t] \to 0$]
A_1 = Solve[[%] == 0, ρ];
Simplify[A_1]

(* Then we do the same thing with the DPE *)

ReplaceAll[A, $S[t] \to \frac{1}{R_N}, Y[t] \to \frac{\alpha}{\lambda}(R_N - 1)$]
A_2 = Solve[[%] == 0, ρ];
Simplify[A_2]

(* What we have done in both A_1 and A_2, are calculate the characteristic equations that we first mentioned in Section 3.4.2. Then we look at both A_1 and A_2 with regard to stability analysis. The majority of this work was done by hand, so it was not necessary to use Mathematica. *)

C.2 Graphs

This is the general program that was used to draw the graphs in Chapter 3. Here we show the code for the *non-vaccinated* system. As mentioned in Section 3.4.6, we used a combination of data from various sources.

Clear[sol]

eqone = $S'[t] == -0.25 * Y[t] * S[t] + 0.02 - 0.02S[t]$;
eqtwo = $Y'[t] == 0.25 * Y[t] * S[t] - 0.02 * Y[t] - 0.1 * Y[t] + 0.002 * L[t]$;
eqthr = $L'[t] == 0.1 * Y[t] - 0.02 * L[t] - 0.002 * L[t]$;

sol = NDSolve[eqone, eqtwo, eqthr,
$S[0] == 70, Y[0] == 23, L[0] == 7$,
$S[t], Y[t], L[t]$, t, 0, 31]

Plot[Evaluate[$S[t], Y[t], L[t]$ /. %], t, 0, 31,
PlotStyle →
RGBColor[0.996109, 0, 0],
RGBColor[0, 0.996109, 0],
RGBColor[0, 0, 0.996109],

Frame → False,
FrameStyle → Automatic,
FrameTicks → Automatic,
DisplayFunction → $ DisplayFunction,
AxesLabel → time, N]

Here we define sols to use NDSolve to compute and then graph a numerical solution to the system.This works by:

- Defining the variables solt, S, Y and t local to the functions sols.
- Defining eqone and eqtwo to be the equations above.
- Defining solt to be a numerical solution to the system above.
- Graphing solt for t in the range [0,30] (* usually *).

Finally, it plots S and Y on the one diagram in the range of t specified.

C.3 Vaccination Level

Below is a table of the various values of λ_V that we used in our *vaccinated* graphs. In the graphs we take a large range of values for λ_V, ranging from the beginning of a vaccination program ($\lambda_V = 3.92$) to the end ($\lambda_V = 0.02$).

ν	$\lambda = 1$	$\lambda = 0.02$	$\lambda = 0.04$	$\lambda = 0.06$	$\lambda = 0.08$	$\lambda = 0.1$	$\lambda = 0.5$
0.01	3.921	0.0784	0.1568	0.2353	0.3134	0.3921	1.961
0.1	3.297	0.0659	0.1319	0.1978	0.2637	0.3297	1.648
0.15	3.008	0.06	0.1203	0.1805	0.2406	0.3008	1.574
0.2	2.753	0.0551	0.1101	0.1652	0.2203	0.2753	1.378
0.25	2.528	0.0506	0.1011	0.1517	0.2023	0.2523	1.264
0.3	2.329	0.0466	0.0932	0.1398	0.1863	0.2329	1.165
0.35	2.153	0.0431	0.0861	0.1292	0.1722	0.2153	1.076
0.4	1.995	0.0399	0.0798	0.1197	0.1596	0.1995	0.9976
0.45	1.855	0.0371	0.0742	0.1113	0.1485	0.1855	0.927
0.5	1.729	0.0346	0.0692	0.1038	0.1383	0.1729	0.865
0.55	1.617	0.0323	0.0647	0.097	0.1293	0.1617	0.8084
0.6	1.515	0.0303	0.0606	0.0909	0.1212	0.1515	0.7577
0.65	1.424	0.0285	0.057	0.0855	0.1139	0.1424	0.7121
0.7	1.342	0.0268	0.0537	0.0805	0.1073	0.1342	0.6708
0.75	1.267	0.0253	0.0507	0.0760	0.1014	0.1267	0.6335
0.8	1.199	0.024	0.0478	0.0719	0.0959	0.1199	0.5995
0.85	1.137	0.0227	0.0455	0.0682	0.091	0.1137	0.5686
0.9	1.081	0.0216	0.0432	0.0648	0.0865	0.1081	0.5404
0.95	1.029	0.0206	0.0412	0.0617	0.0823	0.1029	0.5145
1	0.9817	0.0196	0.0393	0.0589	0.0785	0.0981	0.4908

Table C.1: Values taken for λ_V

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